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## REACTIONS OF THE HEMOPOIETIC SYSTEM TO AGENTS USED IN THE TREATMENT OF DERMATOSES

### EFFECTS OF LOW VOLTAGE ROENTGEN RAY THERAPY

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Heineke<sup>1</sup> was apparently the first to report that roentgen rays and rays from other radioactive substances can damage the hemopoietic organs, his extensive investigations were made on experimental animals. It is also known that radiation may be deleterious to normal human hemopoietic tissue. This knowledge has been gleaned chiefly from studies made on the personnel of diagnostic and therapeutic roentgen ray laboratories<sup>2</sup> and from observations made on persons exposed in industry.<sup>3</sup>

Repeated accidental exposures of human beings to roentgen rays, radium and other radioactive substances, such as occur in the course of some occupations, have resulted in atrophic and hyperplastic changes in the hemopoietic system. The following alterations in the hemogram have been reported: (a) mild leukopenia with relative lymphocytosis, (b) neutropenia, which may develop into agranulocytosis and cause death, (c) aplastic anemia, (d) thrombopenia, (e) leukocytosis and leukemoid reactions, and, (f) leukemia.

Reports on the deleterious effects of therapeutic irradiation on normal hemopoietic tissue are few. In an excellent review of the subject, Dunlap<sup>4</sup> commented, "In spite of the hazard of blood damage as an undesirable side effect

of radiation therapy, few concise data are available on the changes in the blood to even from standardized radiologic procedures. The alterations in the hemogram that result from one or two intensive treatments with roentgen rays have been reported by Minot and Spurling,<sup>5</sup> who made a study of 42 patients before and after irradiation. They found that the white blood cell count fell to its lowest point about six days after irradiation, at which time a count below 5,000 per cubic millimeter was obtained in most of the cases. The leukopenia lasted for an average of about nine days (but could persist over four weeks) and the blood gradually returned to normal if the patient was not reexposed to radiation. The qualitative as well as a quantitative study of the hemogram. Within the first three days after irradiation, the blood contained marked leukocytosis, often amounting to 20,000 or more of the leukocytes, together with some eosinophils. Minot and Spurling found eosinophilia (counts of 7 to 23 per cent) after a usual occurrence two to three days after irradiation. Important changes in the red blood corpuscle counts and the hemoglobin percentage did not occur. Boel<sup>6</sup> reported similar changes in the white cells after exposure to high voltage roentgen rays. In addition to leukopenia and a shift to

From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University.



found quantitative and qualitative changes in the red blood corpuscles. These changes included a drop in the erythrocyte count, sometimes as much as 30 per cent, accompanied with polymorphonuclear leukocytosis, anisocytosis, poikilocytosis, the occasional presence of immature erythrocytes and after a drop in the hemoglobin level.

Gloor and Zuppinger<sup>3</sup> reported the effects of protracted fractionated treatment (Coutard clinic) on the hemogram. They noted initial leukocytosis during the first few days followed by slowly developing moderate leukopenia, with good pictures which did not return to normal until two to four months after treatment had been discontinued. Qualitative changes in the white cells were slight, as were the qualitative and quantitative changes in the red cells. Roentgen rays produced by 8 or 10 kilovolts (grenzys) likewise resulted in leukopenia, associated with a shift to the left.<sup>9</sup>

There has been much speculation about the pathogenesis of the altered peripheral blood picture following irradiation. Dunlap<sup>4</sup> has expressed the opinion that "most of the changes in the blood picture after irradiation of tissues are due to a combination of direct and indirect damage to the blood-forming organs, while destruction of circulating cells plays only a minor role." According to Dunlap, the degree of change in the hemogram and the rate at which the change develops depend on a number of factors: (1) the dose of radiation absorbed by the subject (the dose in turn depending on the number of roentgen units delivered and the size of the field exposed), (2) the minute intensity of radiation (Holthusen<sup>10</sup> presented graphs indicating that 100 r delivered in one minute produces the same biologic effects as 900 r given in fifty minutes or 1,400 r given in eight hours), (3) the effect of wavelength of radiation on biologic processes, (4) individual variations in radiosensitivity (it is estimated that there is about 20 to 30 per cent variation among members of the same species), and (5) the part of the body that is irradiated—for example, high voltage irradiation of the abdomen has been found to produce greater changes in the blood than treatment of the chest, the head and the extremities.<sup>11</sup>

Deleterious effects on hemopoietic tissue from some radiation technics used in the treatment of cutaneous disease have been described. Sommerville<sup>12</sup> found changes in the hemogram resulting from the treatment of dermatoses by means of general roentgen ray baths. The body was divided into two or four large fields. Radiation of 200 kilovolts and 15 milliamperes was used, filtered through tin (0.15 mm), copper (1.15 mm) and aluminum (3 mm) at a focus-skin distance of 200 cm or filtered through copper (1 mm) and aluminum (1 mm) at a focus-skin distance of 90 cm. In 5 patients treated by these methods there developed anemia resembling pernicious anemia, profound leukopenia and extreme lymphopenia. Cipollaro<sup>13</sup> has cautioned against the indiscriminate use of radium compounds or radon in the treatment of cutaneous diseases because of sequelae in the blood-forming tissues.

We have not found reports of changes in the hemopoietic organs or the circulating cells resulting from fractional doses of low voltage roentgen rays, the form of therapy generally employed by the dermatologist in the treatment of cutaneous diseases. While caution in the employment of low voltage radiation is often voiced in clinical presentations and associated effects on hemopoietic tissues are occasionally mentioned in textbooks and published case reports, we have been unable to find any paper devoted to this subject.

The purpose of this paper is to present the effects of the usual forms of therapy of low voltage roentgen rays on the hemograms of patients treated for generalized dermatoses. The effects of both filtered and unfiltered low voltage roentgen rays will be included, also, the effects of low voltage roentgen rays combined with arsenotherapy, since this form of combined therapy is sometimes used by dermatologists in the treatment of chronic dermatoses.<sup>14</sup>

#### MATERIAL AND EXPERIMENT

The patients for this study were selected over a period of four years. Eight patients with generalized dermatoses of various types (4 with mycosis fungoides,

12 Sommerville, J. General X-Ray Baths in Generalized Dermatoses, *Brit J Dermat* **54** 234 (Aug-Sept) 1942.

13 Cipollaro, A. C. Dangers Incident to the Indiscriminate Use of Radium Compounds or Radon in the Treatment of Cutaneous Disease, *J A M A* **115** 1996 (Dec 7) 1940.

14 Herxheimer, K., and Martin, H. Mycosis Fungoides, in Jadassohn, J. *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1929, vol 8, pt 1, p 259. Wise, F., and Sulzberger, M. B. *Year Book of Dermatology and Syphilology*, Chicago, The Year Book Publishers, Inc., 1940, p 371.

3 Gloor, W., and Zuppinger, A. Blutuntersuchen bei protrahiertfraktionierter Bestrahlung, *Strahlentherapie* **40** 438, 1931.

9 Bohm, A. Blutbildveränderungen nach Buckystrahlungen, *Strahlentherapie* **35** 592, 1930.

10 Holthusen, H. Vergleichende Untersuchungen über die Wirkung von Röntgen- und Radiumstrahlen auf die Blutzellen, *Strahlentherapie* **46** 273, 1933.

11 Heim, K. Blutveränderungen bei der Grossfeldbestrahlung, *Arch f Gynäk* **116** 291, 1922-1923.

1 with psoriasis, 1 with generalized sarcoidosis, 1 with lymphosarcomatosis and 1 with multiple idiopathic hemorrhagic sarcoma) were selected. The patients were observed and treated in the Outpatient Department of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital when ambulatory and in the New York Post-Graduate Medical School and Hospital when hospitalized.

Low voltage roentgen rays were administered in accordance with the technic of MacKee<sup>15</sup>. As a rule, three treatments were given each week for a maximum of eight weeks. Approximately 6 fields were exposed at the time of each treatment. Seventy-five roentgens of unfiltered rays ( $\frac{1}{4}$  erythema dose) was administered to each irradiated field at a focus-skin distance of 16 cm, 3 milliamperes of current and 100 kilovolts being used for thirty seconds. When filtered radiation therapy was indicated, 1 or 3 mm of aluminum was used, unless otherwise specified in the case abstracts. The filtered rays were given at a focus-skin distance of 25 cm with a current of 5 milliamperes and 137 kilovolts. As a rule, filtered rays were administered to circumscribed areas, and the average dose was  $\frac{1}{2}$  or 1 erythema dose. An erythema dose with 1 mm filtration is equivalent to 450 r and with 3 mm filtration to 550 r.

In 4 of the cases arsenic was administered either concomitantly or alternately with radiation in the form of daily subcutaneous injections of 2 per cent solution of sodium arsenate, N F. The initial dose was 3 minims (0.18 cc), followed by a daily increment of 1 minim (0.06 cc) and continued until symptoms of intolerance appeared.

For ambulatory patients the blood counts were made in the hematology laboratory of the Skin and Cancer Unit, which is under the direction of one of us (Pascher). When the patients were hospitalized the blood counts were made in the hematology laboratory of the New York Post-Graduate Medical School and Hospital. A count was made before treatment was started, repeated at intervals during the course and again after therapy was discontinued. All blood counts were made prior to roentgen ray treatment in order to exclude immediate transitory effects, since transitory stimulation of the bone marrow following irradiation has been described by a number of observers.<sup>16</sup> The study was limited to the leukocytes, erythrocytes and the hemoglobin content of the red blood cells. Particular attention was given to possible quantitative alterations in the total red cell count and quantitative changes in the total and differential white cell counts. Erythrocyte and leukocyte counts were made with a standard hemocytometer, and the hemoglobin content of the cells was measured with a Sahli hemoglobinometer. Differential leukocyte counts were made from dried blood smears treated with Wright's stain.

#### REPORTS OF CASES AND HEMATOLOGIC OBSERVATIONS

CASE 1—R. R., a woman aged 51, was admitted to the hospital, complaining of a generalized pruritic eruption of five months' duration. The eruption of erythematous infiltrated plaques was distributed on the face, trunk and extremities. The clinical diagnosis of

15 MacKee, G. M. *X-Rays and Radium in the Treatment of Diseases of the Skin*, Philadelphia, Lea & Febiger, 1938.

16 Herzfeld, E., and Schinz, H. R. *Blut- und Serumuntersuchungen unmittelbar vor und nach Röntgenbestrahlung, Strahlentherapie* 15:84, 1923.

mycosis fungoides was confirmed by histologic examination.

On the patient's admission the erythrocyte count was 5,100,000 cells per cubic millimeter, and the hemoglobin level was 74 per cent. One month after roentgen ray therapy was started and 8,025 unfiltered rays had been given, the hemoglobin level dropped to 65 per cent and the leukocyte count dropped from 6,150 to 4,950 cells per cubic millimeter. The red blood cell count and the hemoglobin level fell no further, despite additional irradiation (4,425 r given over a period of four more weeks), but the white blood cell count dropped to 3,000. Treatment was discontinued because of the leukopenia. Twelve days later, the white blood cell count rose somewhat, and after three weeks it was 5,000, which is within normal limits.

CASE 2—J. R., a man aged 40, was admitted to the hospital on April 1943, with a clinical diagnosis of generalized psoriasis. The diagnosis was confirmed by microscopic examination of a biopsy specimen. Laboratory investigation did not disclose any abnormality in the urine or chemical composition of the blood.

In this patient leukopenia developed after two months of treatment with roentgen rays. The leukocyte count on his admission was 7,850 cells per cubic millimeter. One month after treatment was started 9,600 unfiltered rays had been given, and the count dropped to 4,750 cells. After two months, when 13,575 r had been given, the count dropped to 4,300 cells. The red cell count and hemoglobin level did not change. Treatment was continued because of the leukopenia. When the patient was again seen, five months later, the count had risen to 8,900 cells.

CASE 3—S. S., a man aged 57, on June 25, 1939, presented a polymorphous eruption of eczematous, nodular, plaque-like and ulcerative lesions. The clinical diagnosis of mycosis fungoides was confirmed by histologic examination. A complete chemical examination of the blood did not reveal any abnormality other than a 3 plus reaction to the Hanger test. A sternal puncture was made on August 6, and the bone marrow was normal. Leukopenia (3,700 white blood cells per cubic millimeter) was present when the patient was admitted to the hospital. The low white blood cell count was attributed to irradiation, since the patient was treated repeatedly with this modality for years prior to admission.

Roentgen ray therapy was resumed six months later when the leukocyte count was 8,250 cells. A drop to 4,250 cells followed within three weeks after 7,800 of unfiltered radiation had been given. Therapy was discontinued, but the leukocyte count continued to drop during the next three weeks, dropping to 3,450 cells. After five months' rest, the leukocyte count was again within normal limits (5,650 cells). This patient had anemia as well as leukopenia. The lowest values of erythrocytes coincided with the lowest values of leukocytes. The red cells dropped from 5,100,000 to 3,300,000 per cubic millimeter, with a proportionate reduction in the hemoglobin level, from 102 to 74 per cent. Recovery from the anemia was evident after six months.

CASE 4—J. L., a man aged 69, registered at the clinic on Nov. 1, 1939, complaining of a generalized eruption of eighteen months' duration. Violaceous dusky red nodules and plaque-like infiltrations of the skin were found on examination. A tentative clinical diagnosis of lymphoblastoma was made. The histologic diagnosis, made from a specimen taken from one of the nodules in November 1939, was leukemia cutis.

tic type. However, the myelogram in March 1940 revealed normal conditions.

The white blood cell count dropped from 6,300 to 4,000 after seven weeks of therapy, during which 17,737 r of roentgen rays filtered through 3 mm of aluminum was given. The red cells dropped from 4,000,000 to 4,200,000, with a corresponding drop in the hemoglobin level from 108 to 86 per cent. The white red blood cell counts began to rise as soon as therapy was stopped, and they were normal within a few months. A transitory lymphocytosis was noted only in the recovery phase.

No essential change in the patient's condition was noted while he was under observation, except that new lesions appeared from time to time. The patient died at Bellevue Hospital in January 1942. A diagnosis of lymphosarcoma was made after an autopsy.<sup>17</sup>

CASE 5—P L, a woman aged 45, was admitted to hospital on Nov 7, 1942 with a widespread nodular eruption. The nodules varied considerably in size, some were as small as 8 mm in diameter, and others were plaque-like, measuring 3 to 4 cm in diameter. The clinical diagnosis of generalized sarcoidosis (Krausmann) was supported by the report of the histologic examination which read "findings consistent with sarcoid." The observations during a subsequent admission of the patient to the hospital, however, were more suggestive of tuberculoid leprosy. The pathogenesis of these multiple epithelioid tumefactions, therefore, remains in doubt.

Roentgen ray therapy, consisting of 13,000 unfiltered and 300 r filtered through 3 mm of aluminum, and 27 injections of 2 per cent solution of sodium arsenate, (405 minims [57 cc]) were administered over a period of 6 months. The hemoglobin level dropped from 80 to 66 per cent and the white blood cell count from 9,800 to 4,000. There was little improvement in the hemogram after a three month rest period. At this time, perisillar and postpharyngeal enlargement of the lymphatic tissue developed. High voltage roentgen ray therapy was employed to relieve the dyspnea and stridor. 1,657 r filtered through 0.5 mm of copper was administered. This treatment was followed by a marked depression in the white blood cell count (4,900 to 500) but not in that of the red blood cells.

CASE 6—D N, a woman aged 44, was admitted to hospital on Jan 18, 1943 because of a generalized erythematous scaly pruritic eruption. The diagnosis of mycosis fungoides was established on clinical grounds and on histologic examination.

Combined therapy was used. After three weeks of treatment, consisting of 2,000 unfiltered r and 126 minims (cc) of sodium arsenate (2 per cent solution), a decrease was noted in the leukocyte count (8,800 to 6,100), in the erythrocyte count (4,800,000 to 3,800,000) and in the hemoglobin level (87 to 75 per cent). After two months of treatment (22,040 r of unfiltered rays and 290 minims [17.9 cc] of 2 per cent solution of sodium arsenate), the white blood cell count dropped to 4,300 but the erythrocyte count and hemoglobin level remained unchanged. Improvement in the hemogram was noted as soon as therapy was stopped, but recovery was slow. The blood picture was not entirely normal six months later, when roentgen ray therapy was resumed. The leukopenia (3,450 cells) and anemia (3,000 cells and 67 per cent hemoglobin) recurred. An additional 6,150 r of unfiltered and 1,548 r of filtered rays were given over a period of four more

months. The blood count was again normal after four months of rest.

CASE 7—E L, a woman aged 29, was first seen in 1930, at which time a provisional diagnosis of mycosis fungoides was made. The patient was lost sight of for ten years. She returned in August 1940, when a diagnosis of mycosis fungoides was established on clinical and histologic grounds. Leukopenia was noted on her readmission to the hospital, which may or may not be attributable to roentgen ray therapy prior to 1940.

The blood count on the patient's admission was as follows: erythrocytes, 4,100,000, hemoglobin level, 76 per cent, and leukocytes, 4,850 per cubic millimeter, with a normal differential count. After three weeks of arsenotherapy (405 minims [25 cc] of 2 per cent solution of sodium arsenate), there was a slight reduction in the total number of circulating cells. Three weeks after arsenotherapy was discontinued, the blood count improved. Filtered roentgen rays (6,470 r) were then administered over a period of three months, followed by a striking reduction in the number of circulating elements: erythrocytes, 2,700,000, hemoglobin level, 60 per cent, and leukocytes, 2,700. The patient was lost sight of until three months later, when there was little improvement in the blood picture.

CASE 8—M S, a man aged 64, was admitted to the hospital on Feb 18, 1944, complaining of weakness, loss of appetite, loss of weight and an eruption of two years' duration. This eruption was made up of discrete purple-blue nodules of variable size on the nose, the left cheek, both hands, both feet and the front of the left leg. Small lymph nodes were palpable in the anterior cervical and axillary chains. The clinical diagnosis of multiple idiopathic hemorrhagic sarcoma was confirmed on histologic examination. Complete physical examination and laboratory investigation failed to reveal the cause of the patient's emaciated condition.

The patient was treated at a number of clinics prior to admission to our hospital. The case abstracts disclosed that high voltage roentgen rays were administered to the cervical, axillary and inguinal lymph nodes in 1941 and again in 1943. As far as we could determine, no roentgen ray treatment was administered in the last few months prior to our initial blood count, which showed borderline leukopenia.

No treatment, other than application of bland ointments, was used until the white blood cell count was normal. After three weeks of roentgenotherapy (3,500 r filtered through 1 mm and 2,192 r filtered through 6 mm), the total white blood cell count dropped from 9,800 to 3,400 per cubic millimeter. Roentgen ray therapy was discontinued at this time, and arsenotherapy was started. After 81 minims [5 cc] of solution of potassium arsenite U S P was given, there was little change in the blood picture.

# SUMMARY

The effects of therapy of low voltage roentgen rays on the circulating cells of the blood of 8 patients have been presented. In 4 cases we were able to observe the effects of roentgen ray therapy combined with arsenotherapy.

Leukopenia<sup>18</sup> was constantly present. In 3 cases (1, 4 and 7) the white blood cell count dropped to 3,000 per cubic millimeter or less.

18. A reduction in the number of leukocytes in the circulating blood below 5,000 per cubic millimeter.

<sup>17</sup> This report was supplied by Bellevue Hospital.

The depression in the leukocyte count appeared after three or four weeks of irradiation, when approximately 8,000 unfiltered r had been administered. When filtered radiation was used, the degree of leukopenia was the same, despite the smaller fields exposed. In all instances the differential count remained unchanged, except for minor fluctuations in the proportion of granular and nongranular elements and a transitory lymphocytosis during the recovery phase in case 4. In 1 case the white blood cell count was normal three weeks after the last roentgen ray treatment (case 1), but in 4 cases (3, 4, 5 and 6) three to five months elapsed before the number of leukocytes returned to normal. In case 3 the leukopenia progressed even after treatment was terminated.

A reduction in the erythrocyte count and the hemoglobin levels was observed in 5 cases (3, 4, 5, 6 and 7). The anemia was of a moderate degree and of the hypochromic type. The lowest values were obtained in case 6, in which the number of red blood cells was 2,200,000, the hemoglobin level 67 per cent and the number of white blood cells 3,450 per cubic millimeter. There were no qualitative changes in the red blood cells.

Radiation and arsenic were administered concurrently in 2 cases and alternately in 2 cases. When arsenic alone was used, a reduction in the white blood cells, red blood cells and hemoglobin content was found (case 7). This is in accordance with the observations of Halter<sup>19</sup>, working under Jessner's direction in the latter's clinic. In the 2 cases in which roentgen rays and arsenic were administered concurrently, we found leukopenia and a reduction in the hemoglobin content in case 5 and a reduction in the hemoglobin content and in the number of erythrocytes and leukocytes in case 6.

<sup>19</sup> Halter, K. Untersuchungen über die Leukocytenzahl bei Darreichung anorganischen Arsens, Klin Wchnschr 15 52 (Jan 11) 1936

We are of the opinion that individual variations in radiosensitivity and dosage are the primary factors in the development of leukopenia and anemia resulting from repeated exposure of the skin to low voltage roentgen rays. The role of individual radiosensitivity becomes apparent when it is realized that we are able to report hematologic changes in so few patients despite the fact that a large number of patients with generalized or widespread dermatoses have been treated just as intensively as these few at our clinic during the four year period covered by this report. No conclusion can be drawn as to the exact dosage required to bring about these changes, since the exposed areas were not measured. Nevertheless, it is clear that the amount of radiation absorbed was considerable since approximately one fourth of the entire cutaneous surface was exposed at the time of each treatment and treatment was repeated three times a week.

#### CONCLUSIONS

1 Low voltage roentgen rays, used in the treatment of generalized dermatoses and administered three times a week to approximately one quarter of the body surface, are harmful to the hemopoietic tissues of radiosensitive patients.

2 Such low voltage irradiation may be followed by leukopenia or by leukopenia and hypochromic anemia. Recovery may not be complete before four or five months.

3 The quantitative changes in the hemogram due to low voltage irradiation are similar to those following high voltage irradiation.

4 The combination of arsenotherapy with roentgen ray therapy may produce leukopenia or leukopenia and hypochromic anemia, similar to the changes produced with roentgen ray alone.

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# INCIDENCE OF DERMATOSES IN OFFICE PRACTICE IN HAWAII

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In 1941 I classified<sup>1</sup> 1,171 consecutive diagnoses made in the office practice of dermatologists in Honolulu. These indicated that the dermatoses seen in Hawaii did not differ greatly from those seen in mainland United States.<sup>2</sup> The purpose of this report is to supplement that series with an additional 2,777 consecutive diagnoses made after the adjustment to war conditions had occurred, and to compare the incidence of certain conditions before the war and during it.

## EXPLANATORY COMMENT

As noted in the previous report,<sup>1</sup> there is a widespread impression that the dermatoses seen in Hawaii are different from those seen on the mainland. Thus, it appears, is not true. There is also a widespread impression that the climate of Hawaii is tropical, or nearly so, and this is likewise not true. Hawaii's climate is subtropical, by which is meant "temperate" in the literal, not the geographic—sense. The temperature at the Weather Bureau in Honolulu has never been below 52 F or above 90 F; it has reached 88 F only five times in forty years, and 85 F only once in the same period. The average daily maximum temperature in each month ranges in the summer from 78 to 84 F, in round numbers, and in the winter from 76 to 80 F; the range of average daily minimum readings for both summer and winter is almost exactly 10 F lower. The relative humidity averages between 66 and 72 per cent at 8 a. m. and between 60 and 65 per cent at noon; the winter figures being only slightly higher than those for summer, during *kona* (southerly) weather, when the trade winds are not blowing, it rises as high as 80 or 90 per cent. The average total rainfall for each month over the past sixty years in Honolulu has been 1.3 inches (3.3 cm) in the summer and 1.8 inches (4.6 cm) in the winter; it is two to three times this in the valley residential districts. The percentage of possible sunshine per month varies from 58 to 69 per cent. Cyclonic storms

are rare; the barometric pressure has not varied more than 0.8 inches (2 cm) in forty years, and in 1940, for example, did not vary more than 0.39 inches (0.99 cm) in any month, with an average monthly variation of only 0.27 inches (0.68 cm). In summary, Hawaii's climate throughout the year around is stable, warm, sunny and moderately humid.

The distribution of dermatoses in this series is undoubtedly affected somewhat by the fact that the office practice referred to is in conjunction with a co-partnership of seventeen physicians, within which patients are freely referred. Some patients are therefore seen who might ordinarily have remained under the care of the family physician, surgeon, gynecologist or pediatrician whom they originally consulted.

As in the previously reported series, a new diagnosis has been recorded only when it was the most severe or serious condition presented by the patient; usually it was the chief complaint. Thus, a patient requesting treatment for acne was recorded as having only acne, even if severe dandruff was also present. Similarly, fungous infections of the feet were recorded only when they constituted the patient's chief complaint.

## INCIDENCE OF DERMATOSES

A general survey of the field by categories reveals (table 1) that infections account for

TABLE 1.—Distribution of Dermatoses by General Categories

Category	Before the War		During the War		Total	
	No.	Per Cent	No.	Per Cent	No.	Per Cent
Infections	385	33.0	653	23.4	1,038	26.0
Pyogenic	(194)	(16.7)	(321)	(11.5)	(515)	(13.0)
Fungous	(191)	(16.3)	(332)	(11.9)	(523)	(13.0)
Seborrheas	151	12.9	343	12.6	494	12.5
Contact dermatitis	98	8.3	315	11.2	413	10.4
Erythema multiforme	65	5.1	192	6.8	257	6.5
Other	477	40.7	1,274	46.0	1,646	41.6
Total	1,171	100.0	2,777	100.0	3,948	100.0

roughly a fourth of all diagnoses, and that they are divided about equally between pyogenic and fungous infections. Unfortunately, no comparable mainland study is available for comparison, and the factors determining this distribution

<sup>1</sup> 1. Arnold, H. L., Jr. Incidence of Dermatoses in Office Practice in Hawaii. A Preliminary Report, Soc. Staff Meet. Clin. Honolulu 7:63 (May) 1941.  
<sup>2</sup> 2. Sohrweide, A. W. Recent Changes in Dermatologic Diagnosis, Arch. Dermat. & Syph. 30:260 (Aug.) 1934.

are too numerous to permit conclusions to be drawn from these figures

In table 2 are shown the most frequently made diagnoses in approximately diminishing order of frequency. As Goodman predicted in 1931,<sup>3</sup> and as both Gilman<sup>4</sup> and Alderson<sup>5</sup> subsequently showed in student health surveys, dermatophytosis ("tinea") of all types heads the list in both

TABLE 2—Incidence of the Sixteen Commonest Dermatoses in the Series

Dermatosis	Before the War		During the War		Total	
	No	Per Cent	No	Per Cent	No	Per Cent
1 Tinea, all types	191	16.5	332	11.9	523	13.2
2 Contact dermatitis	98	8.3	210	7.6	308	7.8
3 Acne vulgaris	54	8.0	182	6.5	276	6.9
4 Neurodermatitis	24	2.0	204	7.3	228	5.7
5 Seborrheic dermatitis	32	2.7	130	4.6	162	4.1
6 Impetigo	51	4.3	98	3.5	149	3.7
7 Dermatitis venenata	36	3.9	105	3.8	141	3.5
8 Urticaria	26	2.2	73	2.6	99	2.5
9 Pityriasis rosea	29	2.5	62	2.2	91	2.4
10 Furuncle	48	4.0	41	1.5	89	2.3
11 Insect bites	26	2.2	62	2.2	88	2.2
12 Atopic dermatitis	26	2.2	59	2.2	85	2.2
13 Verruca vulgaris	32	2.7	52	1.9	84	2.1
14 Cancer	25	2.1	40	1.4	65	1.6
15 Herpes simplex	24	2.0	40	1.4	64	1.5
16 Miliaria rubra	26	2.2	30	1.1	56	1.3

periods studied, at an average level of over 13 per cent of all diagnoses. The incidence of tinea of the feet alone as a presenting complaint, however, averaged only 3.8 per cent, a figure well below that reported for most sections of the mainland.<sup>6</sup> The actual incidence, of course, is undoubtedly much higher than this, but it is apparent that there is little or no foundation for the popular supposition that this disease is abnormally prevalent in Hawaii.

The only really startling discrepancy between the prewar and war periods is the increase of the incidence of circumscribed neurodermatitis from 2 per cent to 7.3 per cent. The diagnosis was based on the finding of circumscribed lichenification of the skin, usually asymmetric in distribution, associated with paroxysmal itching. Whether this increase proves that the disease becomes more frequent in periods of general emotional stress, or that emotional stress has become more general in Hawaii than it was prior to the

war, would seem to depend on one's preconceptions of the matter.

Table 3 lists the ten most common dermatologic diagnoses made in mainland United States as compiled by Sohrweide<sup>2</sup> from nearly one and a quarter million diagnoses from eight sources, and gives in a parallel column the relative incidence in Hawaii. No comparative incidence is given for his most common diagnosis, "eczema," because it is impossible to sure what that term included, presumably many cases so diagnosed were fungous infection; some were perhaps stasis dermatitis, many were atopic dermatitis and most perhaps were contact dermatitis. The surprisingly poor showing made by tinea in Sohrweide's list may be partly due to the omission of Goodman's statistics from the New York Skin and Cancer Hospital, which indicated a sharp increase in the incidence

TABLE 3—Mainland Statistics After Sohrweide, 1901-1933, Compared with Corresponding Figures for Hawaii

Diagnosis	Least per Cent	Average per Cent	Highest per Cent	Per Cent in Hawaii
1 "Eczema"	15.9	22.7	26.3	
2 Acne	4.0	8.5	13.0	6.9
3 Scabies	2.1	4.5	7.9	0.9
4 Impetigo	0.9	4.2	9.6	3.7
5 Psoriasis	2.8	4.0	7.2	0.9
6 Seborrheic dermatitis	1.1*	3.8	5.1	4.1
7 Urticaria	1.8	3.7	5.1	2.5
8 Dermatitis venenata	1.6†	5.0	17.9(5.0)†	3.5
9 Tinea	0.9	3.4	10.2(3.2)†	13.2
10 Pruritus	0.8	1.1	1.8	0.6

\* Not enumerated among first ten diagnoses by one source.

† Highest and second highest.

‡ Exclusive of (chronic) contact dermatitis.

of tinea in 1929, up to 10 per cent, or 29.0 odd cases, with "eczema" down to 11 per cent and acne at about 8 per cent.

It is interesting to note that acne appears to be about as common in Hawaii as on the mainland, for it is a commonplace observation that acne often has its onset shortly after arrival in Hawaii, in persons not previously so afflicted. Conversely, residents of Hawaii who go to the mainland often observe decided improvement in a preexistent acne without treatment, lasting as long as they remain there.

The incidence of psoriasis in Hawaii, between one third and one eighth of the reported mainland incidence, is low, and this report merely confirms a long-standing general impression of that effect. Whether the incidence of psoriasis in areas with a comparable percentage of possible sunshine is equally low, or whether other factors are involved, I do not know.

It is of interest that neither the emotional stress incident to war conditions nor the great influx of war workers from the mainland appear to have affected its incidence appreciably.

3 Goodman, H. Tinea, the Second Most Prevalent Disease of the Skin, Arch Dermat & Syph **23**:872 (May) 1931.

4 Gilman, R. L. Incidence of Skin Diseases in a Student Health Service, Am J M Sc **188**:268 (Aug) 1934.

5 Alderson, H. E., and Reich, A. Incidence of Dermatoses in a Student Health Service, Arch Dermat & Syph **36**:57 (July) 1937.

6 Investigations Concerning Actual Methods Employed in the Management of Common Dermatoses, J Invest Dermat **3**:523 (Dec) 1940.



is 0.8 per cent before the war and 0.9 per cent during the war period.

Scabies is less frequent in this series than in Sohrweide's list, but this may represent in part at least a difference between its incidence in clinic practice and its incidence in private office practice. "Pruritus" seems less common, but this may be attributable in part to interpretation of terms. Sohrweide's low figure for "tinea" has been discussed previously. The remaining diagnoses in his list—impetigo, seborrheic dermatitis, urticaria and dermatitis venenata—seem to be roughly as frequent here as in the clinics from which Sohrweide compiled his report. Impetigo in this series would occupy a level equal to Sohrweide's highest figure for it if 67 cases of impetiginous dermatitis and 29 cases of lympha had been included. The former, being such a poorly defined entity, was not included in table 2.

TABLE 4—Incidence of Five Dermatoses in the Japanese

Dermatosis	Japanese Cases	Other Cases	Per Cent Japanese
Epithelioma of the skin	0	65	0
Seborrheic dermatitis	57	147	28
Contact dermatitis	63	142	32
Urticaria	11	19	37
Psoriasis areata	14	15	49

It is noteworthy that the fourteenth dermatosis in Hawaii in order of frequency in this series (table 2) is cancer of the skin. Only 2 of the recorded cases were (malignant) melanomas, the remainder were all epitheliomas, and the diagnoses were all confirmed histologically. Only 1 diagnosis of pemphigus vulgaris was made, and a survey of the records of The Queen's Hospital since 1928 revealed only 1 case of this disease. It appears that pemphigus is decidedly less common here than in the temperate zone of the inland United States. This opinion is borne out by statements of other dermatologists.<sup>7</sup>

#### DERMATOSES IN THE JAPANESE

This series of cases is not large enough to permit evaluation of racial distribution of dermatoses. Only the Japanese occur in sufficient numbers to permit a comparison. Table 4 shows the incidence of five cutaneous diseases in Japanese patients as compared with their total incidence. Japanese constitute about 35 per cent of the population of Honolulu and about 30 per cent of the total clientele of our group. It will be noted that significant deviation above or below the average figure occurred in only two dermatoses, psoriasis areata, half the patients being Jap-

anese, and epithelioma of the skin, none of the patients being Japanese.

This apparently low incidence of epithelioma of the skin in Japanese was investigated further. In over five years of practice in Hawaii I had seen only 4 cases, all of which were proved histologically. A simple questionnaire was sent out requesting an answer of yes or no to the question "Have you even seen a case of skin cancer in a Japanese patient?" Ninety non-Japanese physicians and twenty-five Japanese physicians replied that they had not. Three Japanese and six non-Japanese physicians replied that they had. Five of the negative replies were of particular interest. Two leprologists, Dr. A. Mouritz and Dr. J. T. Wayson, each with approximately fifty years of experience in medical practice in Hawaii, replied that they had never seen cutaneous cancer in a Japanese, two surgeons, Dr. James R. Judd and Dr. J. E. Strode, with forty-one and twenty-two years of practice here respectively, had never observed it, and one dermatologist, Dr. Harold M. Johnson, with nearly three years of experience here, had not seen such a case. It is apparent from this that the susceptibility of the Japanese to cancer of the skin is extremely slight.

The reason for this is not at all clear. It is not merely a matter of degree of pigmentation of the skin, for Japanese are no more deeply pigmented than the Chinese and less so than most Hawaiians, yet these groups are not by any means immune. It is not a question of lack of opportunity of exposure to sunlight—rather the reverse, for the fishing and farming of the Territory of Hawaii have been largely dominated by Japanese for the past several decades. It is not peculiar to Hawaii, for Dr. H. E. Bowles informed me that when he was practicing in Japan he saw only 1 case of epithelioma of the skin in a Japanese, a man of 56 with multiple lesions, and that case was being presented by a dermatologist, Dr. Iida, as a pathologic curiosity from the standpoint both of his multiplicity of lesions and of his race. Very likely this peculiar freedom of the Japanese from cutaneous epithelioma has been reported previously, but I have found no record of it.

#### DERMATOSES OF SPECIAL INTEREST

Certain dermatoses, not common enough for statistical evaluation of their incidence in this small series, require special mention here.

Eighteen cases of leprosy were seen, of which 10 had not been previously diagnosed, the other 8 were seen in consultation or for special study. Only 2 cases were of the lepromatous type, the remainder were "neural" cases. Of these 2 were

<sup>7</sup> Wayson, J. T., and Johnson, H. M. Personal communications to the author.

of special interest in that they were not only "neural" in type but neural in involvement as well, that is, they were so-called neural anesthetic or "Na" cases, one without any cutaneous manifestations and the other with purely trophic ones. The former subsequently became an outspoken "Nt" or "neural tuberculoid" case. No case of "mixed" leprosy in the sense of combined lepromatous and "neural" types was seen, though every case was studied from both clinical and histologic standpoints. Both of the lepromatous cases were "mixed" in the sense that both presented the usual combination of cutaneous and neurologic changes, with thermal and tactile hypesthesia and anesthesia, enlarged nerve trunks and muscular weakness and atrophy. Seven of the 18 cases occurred in Hawaiian or Caucasian-Hawaiian patients, 3 each in Filipino and in Japanese and the remainder in 2 Portuguese, 1 Puerto Rican, 1 Samoan and 1 Chinese patient.

Twenty-six cases of discoid lupus erythematosus were seen, an incidence of about 0.7 per cent. It is of at least passing interest that the immunity of Japanese to one disease brought on or aggravated by sunlight cancer of the skin does not include immunity to this disease. Six of the cases occurred in Japanese, 7 in Chinese and the remainder in Caucasians. Two of the 26 cases, one in a Portuguese woman and the other in a Chinese girl, subsequently became disseminated and ended fatally.

Twenty-two cases of fungous infection of the scalp were seen, all in children. *Trichophyton crateriforme* was cultivated in 1 case, *T. gypseum* in 4 cases, *T. sulfureum* in 1 case and *Microsporum lanosum* (felineum) in the remainder, except for 2 cases in which cultures were sterile. *M. audouinii* was not cultivated from any patient. The cases of *lanosum* infection were usually non-inflammatory, perhaps 1 in 4 was kerion-like when first seen.

The relative infrequency of lichen planus in Hawaii has been remarked on by at least two observers.<sup>7</sup> Only 2 cases of it occurred in the prewar period of this series and 5 in the war period—a total of 7 out of nearly 4,000 cases.

## SUMMARY

Two series of consecutive diagnoses made in the office practice of dermatologists in Hawaii have been reviewed, including a total of 3,945 cases.

The most frequently made diagnoses were dermatophytosis, with an incidence of 13 per cent of all diagnoses, and pyogenic cutaneous infections, including all varieties, which were equally common.

The ten most common dermatoses diagnosed were, after tinea, contact dermatitis, acne vulgaris, circumscribed neurodermatitis, seborrheic dermatitis, impetigo contagiosa, dermatitis venenata, urticaria, pityriasis rosea, furuncle and insect bites.

The only striking difference between the prewar and wartime series was the rise of circumscribed neurodermatitis from eleventh place (2.0 per cent) to third place (7.3 per cent).

Psoriasis constituted slightly less than 1 per cent of all the diagnoses made in this series, though on the mainland it varies from 2.8 to 7 per cent.

Only 1 case of pemphigus vulgaris, a fatal case in a Japanese man, was seen during the period studied, and inquiry revealed evidence of only 1 other case ever having been observed in Honolulu.

No case of cutaneous epithelioma in a Japanese was observed during the period studied, and inquiry revealed that this disease is rare.

## CONCLUSIONS

Dermatophytosis is the most common dermatosis met with in the office practice of dermatologists in Hawaii.

Psoriasis is between one third and one eighth as frequently seen in Hawaii as on the mainland.

Pemphigus vulgaris is rarely seen in Hawaii.

Epithelioma of the skin appears to be relatively common in Hawaii, but is rarely seen in the Japanese.

Tinea of the feet is less common in dermatologic practice in Hawaii than on the mainland.



# RECURRENT, FIXED ERYSIPELAS-LIKE DERMATOPHYTID

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The development of inflammatory plaques on lower extremities as a complication of dermatophytosis of the feet is well known. After Glasson<sup>1</sup> in 1926 called attention to the phenomenon, it was presumed that the lesions on the feet and legs were areas of erysipelas or cellulitis caused by lymphatic transmission of bacteria, usually hemolytic streptococci, which passed through fissures and erosions of fungous origin situated between the toes and on the soles. According to this view, the fungi on the feet are passive actors in a dramatic episode, serving the usual role of throwing open the portals for bacterial penetration into deeper tissues and lymphatic channels, while they themselves remain standers, and often inconspicuous ones. The concept has much clinical evidence to support it, and at the present time it is widely held. Added support for this mechanism is provided by the efficacy of adequate treatment of the focus of dermatophytosis in preventing recurrences of the erysipelatos eruption on the extremities.

Traub and Tolmach<sup>2</sup> and Sulzberger, Rostenberg and Goetze<sup>3</sup> first suggested that erysipelas-like exanthems on the feet and legs might represent a complication of fungous hypersensitivity. Based on illuminating clinical and immunologic observations, this theory postulated that an allergic response to fungous toxins emanating from foci on the feet and toes rather than direct bacterial infection produced the eruption. The authors were careful to state that while the evidence favored interpretation of the lesions as

dermatophytids they did not deny the possibility that some might be caused by streptococci and therefore be true recurrent erysipelas and also that some might be caused by a combination of fungi and streptococci.

The following features of differentiation of the erysipelas-like dermatophytid from true erysipelas, quoted from Traub and Tolmach,<sup>2</sup> indicate concisely the general clinical properties of the disease under consideration.

The erysipelatos "id" is usually found near a focus of fungous infection. The temperature is no guide, for it may be normal or as high as 104 F. There is not the definitely sharp margin or the progressive spreading of the lesion as in true erysipelas. There may be two separately involved areas present at the same time, such as in the two legs, in cases of erysipelas-like "id." The glazed appearance and brawny induration of erysipelas is not characteristic of these cases. Nor are apparent foci of pyogenic infection found. A history of many and in some cases frequent recurrences is the rule. Constitutional symptoms are comparatively mild and of short duration. Fatalities have not been seen.

The belief that the dermatophytid may be incriminated as a common manifestation of recurrent inflammatory lesions on the lower extremities has been challenged by a few dissenting observers.<sup>4</sup> Yang<sup>5</sup> declared that the great majority are due to streptococcic infections (erysipelas) and that only a few are dermatophytids. He added "If those cases of cellulitis, lymphangitis and single attacks of erysipelas are included, the percentage of streptococcus infection complicating epidermophytosis of feet will be much higher." Goeckerman and Wilhelm<sup>6</sup> expressed the conviction that the erysipelatos syndrome was entirely and invariably caused by bacteria (streptococci and occasionally a mixed infection with staphylococci), that because of a

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<sup>1</sup> McGlasson, I. L. Recurrent Erysipelas of the legs with Dermatitis of the Feet, *Arch Dermat & Syph* **14** 679-681 (Dec) 1926.

<sup>2</sup> Traub, E. F., and Tolmach, J. A. Dermatomycosis, in *Deliberationes Congressus Dermatologicum Internationalis IX*, Budapest, Institutum Typographicum "Patria" S. A., 1935, pp 714-719, An Erysipelas-Like Eruption Complicating Dermatophytosis, *J A M A* **108** 2187-2189 (June 26) 1937.

<sup>3</sup> Sulzberger, M. B., Rostenberg, A., Jr., and Goetze, D. Recurrent Erysipelas-Like Manifestations of the Legs. Their Relationship to Fungous Infections of the Feet, *J A M A* **108** 2189-2193 (June 26) 1937.

<sup>4</sup> Recurrent Erysipelas-Like Eruptions, Queries and Minor Notes, *J A M A* **122** 778-779 (July 10) 1943.

<sup>5</sup> Yang, K. L. Causal Relationship Between Epidermophytosis of Feet and Recurrent Erysipelas and Elephantiasis of the Legs, *Chinese M J* **57** 161-167 (Feb) 1940.

<sup>6</sup> Goeckerman, W. H., and Wilhelm, L. F. X. Recurrent Lymphangitis. Report of a Case with Unusual Features, *California & West Med* **55** 251-252 (Nov) 1941.

change in the patient's immunity the activity of the bacteria remained confined to a localized area of the lymphatic bed, and that fungous allergy was not involved at all

I believe the latter view to be extreme. The erysipelas-like dermatophytid, although uncommon, has distinct biologic features which set it apart from erysipelas. It is the purpose of this paper to review some of these fundamental differences in an effort to crystallize a clinical concept of the dermatophytid.

#### REPORT OF A CASE

The following case is presented as a basis for discussion of erysipelas-like eruptions caused by dermatophytosis. It is of interest because of the long duration of the disease, the multiple recurrences, the singular location of the eruption, the regional hypersensitivity to trichophytin and the favorable influence on the recurrences of topical therapy directed toward the eradication of the fungous infection.

*History*—A soldier, 32 years old, was seen on April 13, 1943 because of an acute inflammatory eruption on the left thigh resembling erysipelas, which had developed the day before. The patient stated that this was the latest of a series of attacks (numbering about seventy-five) of dermatitis in the identical area of the thigh which had recurred repeatedly during the previous five years. For the first two years attacks had occurred at average intervals of two or three weeks, and then for a period of over a year in 1940 and 1941 he had been free of the disease. But since July 1942 recurrences had appeared every two to five weeks, and during the month previous to admission they had come at approximately weekly intervals.

According to the patient's description, the sequence of events for each attack was practically uniform. He could anticipate the eruption by the onset of a sensation of tenseness and aching in the left thigh a day or two prior to the development of the lesion. The acute disease was usually ushered in with a headache and a feeling of chilliness or actual chills, followed as a rule by fever and shortly afterward by the appearance of a painful eruption over the thigh, which rapidly spread to definitive size within a few hours. Simultaneously, a tender enlarged sublingual lymph node would present itself. During the next forty-eight hours the fever would abate (without treatment aside from rest in bed), and within a day or two the cutaneous lesion would have disappeared, the lymph node would have subsided and the patient would be entirely well.

*Examination*—The patient appeared moderately ill, but he had no fever. He walked with a limp, the left thigh flexed at the hip and the knee bent. Over the lower two thirds of the left thigh, on its medial surface, was a large, roughly quadrangular, dull-hued, diffusely erythematous plaque, measuring 16 by 20 cm, with irregular and festooned outlines (fig 1). The border of the affected area was slightly elevated and the surface shagreened, and small islands of dermatitis of similar appearance were scattered peripherally. The lesion was hot to the touch and tender. There were no signs of phlebitis or lymphangitis. A sublingual lymph

node was enlarged and sensitive. At this examination there was noted a mild grade of scaling and vesicular dermatophytosis on the feet.

The erythrocytes numbered 4,150,000 per cubic millimeter of blood, the hemoglobin content 14 Gm per hundred cubic centimeters and the leukocytes 5,900 per cubic millimeter, with 61 per cent neutrophils and 3 per cent lymphocytes. Examination of the urine disclosed no abnormality, and the Kahn test of the blood elicited a negative reaction.

By the next day the erythema of the lesion had faded leaving a faint grayish tan pigmentation, without trace of edema.

*Subsequent Course*—The patient was readmitted to the hospital on May 2, 1943, with temperature 101 F, the same appearance and distribution of the eruption and left sublingual lymphadenitis. The leukocyte count was 7,200 cells per cubic millimeter of blood, with 74 per cent neutrophils and 26 per cent lymphocytes. To permit observation of the spontaneous course of the eruption, medication was withheld. Two days later



Fig 1—Recurrent, fixed erysipelas-like dermatophytid of twenty-four hours' duration. Outlines of the erythematous plaque are indicated by arrows. (Reproduced from kodachrome transparency.)

the patient was afebrile, and the lesion had faded, leaving a faint pigmentation to mark the involved area.

June 8, 1943 he was admitted again to the hospital with temperature of 102.2 F, pulse rate 84 and leukocyte count of the blood 7,700 cells per cubic millimeter. The lesion on the thigh and the regional lymphadenitis were identical with those of previous attacks. There were a moderate grade of scaling and maceration between the toes and a few scattered tiny vesicles on the soles, in which numerous myceliums were demonstrated by microscopic examination. Within twenty-four hours the patient became afebrile, central involution of the lesion was well advanced and the sublingual node, although still enlarged, no longer felt sensitive to pressure.

During the following month three "abortive" attacks were observed, in which the maximum elevation of temperature was 99.8 F. In each instance the skin returned practically to normal within twenty-four hours. During this period, sulfonamide prophylaxis was attempted and found to be ineffective.

July 26, 1943 the patient was observed again, with recurrence of the acute inflammatory plaque. His temperature was 100 F. Over the left thigh spread the familiar, irregularly outlined, hot, dusky, rose-hued, slightly elevated lesion covering the distal two thirds lateromedially, with small islets of erythema scattered about the periphery. A soft, tender lymph node, measuring 2 by 4 cm, was palpated in the femoral triangle. There was nothing indicative of phlebitis, lymphangitis or lymphedema. Studding the right instep was a cluster of a dozen "sago grain" vesicles, and a few similar vesicles were found on the under surfaces of the left first and third toes. The sides of the lateral three toes on each foot were occupied by macerated and scaling dermatitis. A deep fissure was present beneath each fifth toe at the plantar-phalangeal crease. The hands and fingers were free of lesions.

The fungous infection of the feet responded sluggishly to topical therapy, necessitating the successive use of a variety of conventional fungicidal agents before being brought under control. In spite of this refractoriness, however, once treatment was instituted there was no recurrence of the lesion on the thigh for a period of four months. The patient was readmitted to the hospital Nov 23, 1943, with mild erysipelas-like dermatitis on the thigh, ascribed to a lapse in the care of his feet. Up to the time of this writing, June 1944, there have been no further seizures.

#### INVESTIGATIVE DATA

**Trichophytin Tests** A trichophytin test, performed with 0.1 cc of antigen (Lederle) injected



Fig 2—Reaction produced by injection of 0.1 cc of trichophytin one hour previously into the "fixed" area of the recurrent lesion on the left thigh. Antigen was introduced at the level of the midthigh, the site marked by the presence of the punctum and wheal. Comparison with figure 3 discloses the tremendously intensified local allergic reactivity.

intracutaneously on the forearm, caused the appearance within thirty minutes of a central wheal with pseudopods and a zone of erythema 1.5 cm wide. The reaction site measured 1.5 cm

in diameter in three, twenty-four and forty-eight hours and exhibited mild infiltration which persisted for about four days. It was graded 1 plus on a scale of 1 to 4. There was no focal lighting-up of the lesion on the thigh following the trichophytin test on the forearm.

Inoculation of trichophytin into the area of the recurrent lesion on the left thigh evoked within thirty minutes a large wheal with pseudopods and a brightly erythematous flare (fig 2). The reac-

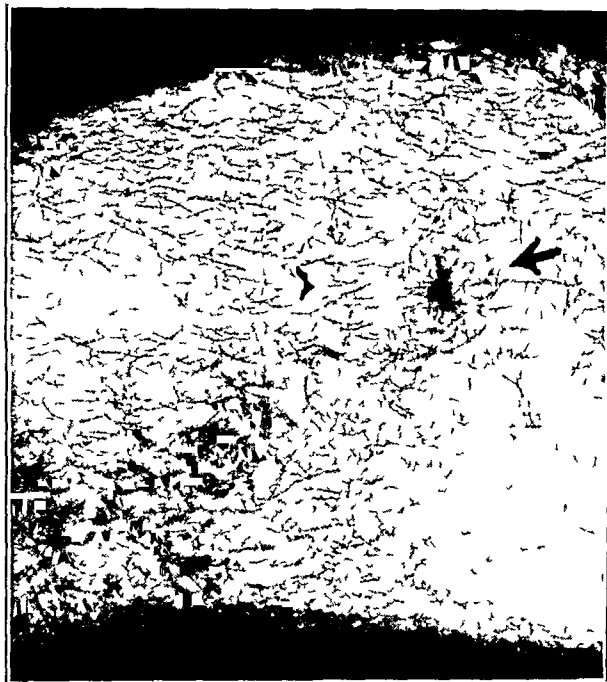


Fig 3—Wheal and erythema produced by injection of 0.1 cc of trichophytin into the medial aspect of the right thigh.

tion covered the area of skin which had participated in the attacks of the past, while the previously uninvolved, adjacent parts were spared, it simulated identically the original recurrent eruption. The erythema receded within two hours to a diameter of 3 cm, but twelve hours later it spontaneously flared up to its initial size and remained visible in this extended form for the following two days. At the point of injection there appeared an infiltrated area 2 cm in diameter, and the left sublingual lymph node became swollen and tender but there was no fever or other constitutional disturbance. By the third day both the cutaneous reaction and the enlargement of the lymph node had subsided almost entirely, the infiltration at the site of inoculation fading out during the next few days.

The trichophytin test was repeated, with duplication of the previous events. In less than thirty minutes the immediate reaction on the left thigh would attain dimensions many times greater than those of a control inoculation with trichophytin on the right thigh (fig 3), and it would

be succeeded by the flare-up twelve hours later. A response could be elicited only by intracutaneous administration of trichophytin, subcutaneous injection into the left thigh caused no reaction.

As a control check on the local reactivity of the skin, solution of histamine acid phosphate was injected intracutaneously into corresponding sites of each thigh medially. The wheal and flare produced over the affected area did not differ from that of the normal skin in size and speed of evolution and decline.

By the Prausnitz-Kustner technic, positive immediate urticarial responses to trichophytin were elicited in the skin of normal persons passively sensitized by intracutaneous injection of the patient's serum. A precipitin test of the patient's serum, 1:30 dilution of trichophytin being used as the antigen, was weakly positive.

It was believed that the question, Is the erysipelas-like eruption provoked by antigen arriving via hematogenous pathways? might be clarified by observing the effect of intravenously administered trichophytin on the trichophytin-hypersensitive region of the left thigh. Accordingly, a series of such injections was given in December 1943, beginning with 0.05 cc and increasing cautiously until 1 cc of the 1:30 antigen was reached, but no reaction occurred, either focally or systemically. However, it was noted after these injections were completed that the second phase of the trichophytin reaction could no longer be elicited—that is, the twelve hour lighting-up of the affected site failed now entirely to develop.

**Trichophytin Hyposensitization** A series of injections of trichophytin, given intradermally into the arms, was started in October 1943. Seven injections had been given when the patient was readmitted to the hospital, on November 23, after a four month interval of freedom from recurrences of the dermatitis. In the absence of obvious protection, it was decided to abandon this form of treatment.

The idea of inducing local hyposensitization next suggested itself, and accordingly a series of intradermal injections of trichophytin was given in the reacting area of the thigh. It was observed at this time that the twelve hour reaction no longer appeared after each injection, as it had previously. Between Jan 15 and Feb 14, 1944, twelve injections of trichophytin (0.1 cc) were given in various parts of the sensitized area. A progressive diminution in size of the immediate reaction occurred, so that by the middle of February the flare measured 6 by 8 cm, an area not much larger than that developing anywhere

else on the skin. The intensity of the forty-eight hour reaction was not visibly affected by the treatment.

**Histopathologic Observations** A biopsy specimen was taken from the lesion at the height of an acute attack (fig 4). The epidermis was normal. In the cutis the collagen bundles were moderately separated by edema. About the vascular structure of the skin centered the conspicuous alterations. The endothelial cells of the blood vessels were swollen, polymorphonuclear leukocytes, occupying the dilated lumens, and a cellular infiltrate surrounded the vessel walls. The infiltrate (comprised of polymorphonuclear leukocytes, lymphocytes, a few histiocytes and scattered eosinophils) outlined several of the horizontal

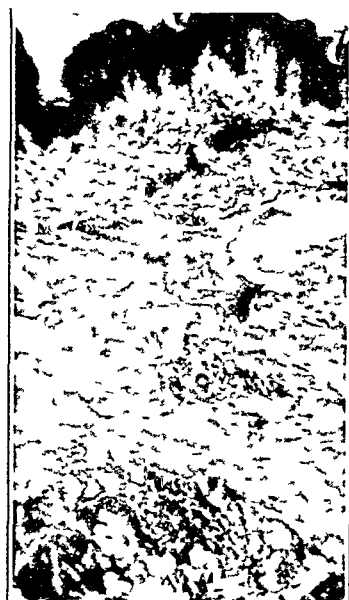


Fig 4—Biopsy from the plaque of recurrent dermatophytid, showing edema and perivascular cellular infiltrate in the cutis.

vessels in the upper part of the cutis, and in addition it sparsely stippled the subpapillary layer. In the deeper part of the cutis a dense collection of cells was distributed both in a perivascular pattern and about the sweat gland. Careful search failed to show bacteria in this section.

**Cultural Results** Culture of a fragment of the biopsy specimen removed from the actively inflamed lesion yielded no organisms. Epidermis from the vesicles on the feet and toes, inoculated on Sabouraud's medium, grew *Trichophyton interdigitale*. Bacterial cultures from the interdigital spaces of the toes resulted in a growth of a coagulase-negative *Staphylococcus aureus*.

#### DIAGNOSIS

The erysipelas-like dermatophytid, as Yang<sup>1</sup> pointed out, is a less intense and more diffuse

erythematous lesion than erysipelas. It appears as recurrent patches of constant size, shape and topographic distribution. Its color is vivid crimson or dusky red, and the borders of the patches not only lack the sharp definition characteristic of erysipelas but also are surrounded by small papules or islands of eruption. There is, in addition, an important triad of negative distinctions from erysipelas and cellulitis. The uncomplicated dermatophytid is never surmounted by vesicles or bullae, it is never associated with lymphangitis, and it is rarely if ever followed by the development of solid edema.

The streptococcal type of inflammatory eruption of the lower extremities and the erysipelas-like dermatophytid may generally be distinguished by certain contrasting characteristics. Suggesting erysipelas are the following features: (1) longer duration of the attack than generally occurs with the dermatophytid, (2) neutrophile leukocytosis, (3) usual coexistence of higher temperature and more pronounced systemic reaction, (4) successful treatment with sulfonamide drugs, and (5) frequent supervention of fibrosis and lymphedema (elephantiasis) as sequelae of repeated infectious episodes.

The foregoing criteria are the reverse of those associated with the dermatophytid, which usually is manifested by (1) rapid evolution and subsidence, at times within twenty-four or forty-eight hours, (2) leukocytosis inconstant and often absent, (3) afebrile course or one associated with relatively low fever and mild constitutional symptoms, (4) failure of sulfonamide therapy to influence the course of an attack or to prevent recurrences, and (5) absence of lymphedema, regardless of multiple and frequent recurrences.

It must be emphasized that the erysipelas-like dermatophytid may recur repeatedly without producing permanent gross changes in the consistency of the reacting skin. When lymphedema appears with the dermatophytid, I should suspect the possibility of coincident or superimposed bacterial invasion. The absence of permanent structural damage is explained by the histologic demonstration simply of edema and perivascular infiltration; sequelae will no more follow such a reaction than they would one of the symptomatic erythemas or fixed drug eruptions. Recurrent attacks of erysipelas, on the other hand, will lead to persistent cutaneous damage. There is no doubt that some cases which have been reported as examples of erysipelas-like dermatophytid are distinctly and exclusively of bacterial origin, as Goeckerman and Wilhelm<sup>7</sup> have properly concluded. Reiss<sup>8</sup> described changes consisting of scaling glossy skin, impetiginous-eczematous

lesions, lichenification and warty papillomatous proliferation, all of which are suggestive sequelae of pyogenic infection. The lesions complicating recurrent erysipelas are generally located in front of the ankle or over the metatarsophalangeal region of the dorsum of the foot, and increased girth of one or both legs is eventually an accompaniment. These are residues of an infectious disease with lymphangitic spread, and they are due to repeated injury of lymphatic vessels by the infecting agent.<sup>9</sup> In the same category falls solid edema of the cheeks subsequent to recurrent erysipelas of the face—a complication, as stated before, altogether foreign to a nonlymphangial disease.

#### COMMENT

I concur with the opinion of Yang<sup>5</sup> that among the inflammatory lesions on the lower extremities complicating dermatophytosis of the feet the incidence of the erysipelas-like dermatophytid is low as compared with that of eruptions caused by streptococci. Deserving attention is the fact that erysipelas itself constitutes by no means the commonest occurrence among the complications induced by bacterial invasion. Lesions on the lower extremities caused by streptococci emanating from foci of dermatophytosis include cellulitis, lymphangitis, superficial phlebitis and erysipelas, and it is my impression from personal observations that, excluding combinations, the incidence of these eruptions is in the order just given. (In addition, an erysipelas-like "streptococcal" may well occur on the lower extremities and elsewhere as a form of allergic response to bacterial products<sup>9</sup>.) It is therefore evident that the erysipelas-like dermatophytid is not a frequent manifestation when the incidence of other inflammatory conditions of the legs is tabulated.

The factors which condition a peculiar allergic predisposition of one well defined, localized area of the skin are imperfectly understood. In the case reported, the patient suffered an estimated seventy-five separate exacerbations of dermatitis, each lighting up unvaryingly at the single site on the left thigh, yet, notwithstanding the five years' duration of recurrent symptoms, there was no spread of hypersensitivity to adjacent or distant

7 Reiss, F. The Relationship Between Chronic Erythematous Dermatitis of the Feet and Recurrent Erysipelas-Like Manifestations, *J Clin Med* 3 13-16 (Jan-March) 1938

8 Allen, E. V. Lymphedema of the Extremities: Classification, Etiology and Differential Diagnosis, a Study of Three Hundred Cases, *Arch Int Med* 54 606-624 (Oct) 1934

9 Amoss, H. A. Treatment of Recurrent Erysipelas, *Ann Int Med* 5 500-504 (Oct) 1931

be seen. Here the strict localization of intense allergic hypersensitivity to fungous products was demonstrated by the remarkable immediate reaction produced by trichophytin when injected into the predisposed zone of the skin, a reaction ten times the size of that elicited at a control site. The positive local trichophytin reaction (employed originally by Sulzberger<sup>3</sup>) reproduced the primary eruption both in extent and appearance and even in the development of regional lymphadenitis. Injection of trichophytin into the skin at a distance failed in my case to provoke a flare-up of the eruption, unlike the focal reaction manifested by 1 patient of Traub and Tolmach.<sup>2</sup> Nor was I able to stimulate the sensitized site to activity by injecting trichophytin intravenously, but this failure does not, of course, impair the hypothesis of a specific allergic mechanism, even of a blood-borne antigen, in the pathogenesis of the isolated inflammatory lesion.

Histopathologic studies of the dermatophytid have not been previously reported. In my case the cutaneous alterations viewed at the height of the inflammation were surprisingly mild. As important changes, the lesion exhibited perivascular clustering of cells, particularly conspicuous in the deeper portion of the cutis, and mild edema throughout the cutis. Microscopic characteristics of erysipelas—dilated lymphatics, heavy polymorphonuclear infiltration, severe edema and demonstrable cocci—were not evident. The picture was one readily identified with the group of "toxic" eruptions.

Bacteriologic studies in this case likewise argue against a diagnosis of pyogenic dermatitis, as shown, first, by failure to grow organisms from the involved tissue itself and, second, by the cultivation only of a presumably nonpathogenic staphylococcus from between the toes. While not conclusive in themselves, these cultural results at least suggest the presence of a non-infective disease and thereby sustain the histopathologic impression. At this point also may be noted the failure of sulfonamide drugs both prophylactically and therapeutically, which is not what one would anticipate in an acute infection caused by hemolytic streptococci. Unsatisfactory results with the sulfonamide drugs have been the similar experience of others.<sup>10</sup>

The immediate whealing response to intracutaneous injection of trichophytin is an uncommon reaction, the significance of which is not clear. Its reaginic nature can be demonstrated by the technic of passive transfer, indicating the presence of specific antibodies in the circulating

blood. From his observations, Marcussen<sup>11</sup> concluded that the immediate and the delayed reactions are produced by the same antigen component and that they both therefore carry the same diagnostic implication. Sulzberger<sup>12</sup> declared that the type of response to cutaneous testing might in some way be related to the clinical form of mycosis, since patients with erysipelas-like dermatophytid and with infections caused by *Trichophyton purpureum* are more likely to show urticarial immediate reactions. The unique reappearance in my patient of the erythematous trichophytin flare-up twelve hours after its initial subsidence on the thigh (but not elsewhere) might be interpreted as the first visible manifestation or "flash" in hypersensitive tissue of the delayed, tuberculin type allergic reaction. In other words, the sensitization here was obviously bivalent, representing an association of both the "urticarial" and the "tuberculin" reaction types intensified inordinately and with explosive manifestations on the left thigh. The twelve hour lighting-up might therefore be explained by hypothesizing the presence in situ of an aberrant fraction of the antibody complex responsible for the tuberculin type reaction or of exaggerated quantities of a normal fraction. Consistent with the theory just advanced, the site of passive transfer studies gave no indication whatever of a twelve hour flare-up, nor was a comparable flare-up demonstrated when the trichophytin test was performed elsewhere on the patient's skin than the affected thigh. As to the cause of the eventual disappearance of the twelve hour reaction, I can only conjecture vaguely that it was brought about by immune biologic changes produced by the intravenous injections of trichophytin.

It follows from what has already been indicated of the background of recurrent erysipelas-like eruptions that treatment should logically be directed toward complete and permanent eradication of the primary dermatophytosis, but the practical difficulties preventing attainment of this ideal are familiar. Obstacles to effective arrest of the dermatophytid are the multiple relapses and reinfections which characterize the superficial mycoses of the feet, as well as the refractoriness of the organisms to chemical disinfection on the skin. Recognizing the limitations of direct or causal therapy, the suggestion has

11 Marcussen, P. V. Relationship of the Urticarial to the Inflammatory Reaction to Trichophytin, *Arch. Dermat. & Syph.* **36** 494-514 (Sept.) 1937.

12 Sulzberger, M. B. *Dermatologic Allergy*. An Introduction in the Form of a Series of Lectures. Springfield, Ill., Charles C. Thomas, Publisher, 1940.



zen offered that measures designed to alter the hyperallergic state of the shock tissue might be more effective in controlling the recurrent dermatophytid, and, indeed, favorable results have been reported from the serial administration of trichophytin. Failure to detect evidence of diminishing sensitivity from routine injections of trichophytin in my case led to the introduction of the antigen directly into the affected site, with resultant prompt and progressive reduction in the intensity of the immediate reaction but not of the forty-eight hour type reaction. (It will be pertinent at this point to recall the principle of allergy that a total disappearance of an immediate wheal reaction cannot be induced by injections of the offending allergen and also that specific hyposensitization may be attained by treatment and yet the positive cutaneous reaction and Prausnitz-Kustner reagins in the blood will persist.) To appraise the practical value of hyposensitization here is difficult in view of the satisfactory results obtained with exclusively local treatment of the dermatophytosis. Sulzberger,<sup>13</sup> however, has witnessed the cessation of acute recurrences of dermatophytid after a course of injections of trichophytin without other treatment.

A lesion which is evolved at an unchanging spot, characterized by repeated exacerbations and probably provoked by a specific biologic agent, speaks an analogy to the fixed form of erythematous drug eruption.<sup>14</sup> The sudden and multiple recrudescences of the fixed drug eruption and the transient pigmentation which is its sequel closely parallel the features of the dermatophytid. Unfortunately, information is meager concerning the biologic processes which govern the remarkable effect of certain drugs on isolated reacting areas of the skin. One may assume for the dermatophytid that the interaction of liberated fungous products with the localized, immunologically altered zone of skin (antigen-antibody union) has the effect of calling forth an acute vascular reaction in situ. Possibly this could be interpreted in the light of the events of the Arthus phenomenon. Circumstances determining a particular flare-up would depend on largely unmeasurable factors, such as a fluctuating degree of cutaneous allergy ("receptivity" of the skin) and the quantity of fungous allergen reaching the reacting tissue. The immunologic phenomena involved intrigue the imagination, particularly when it is considered that the exciting focus of

dermatophytosis on the feet is often of trivial grade. As for the dissemination of the fungous products to the hypersensitive area, it is not clear whether this proceeds by the hematogenous route or by way of lymphatic channels or by both. All three means of dissemination have been shown to occur in "ids" of other types. The frequency at least with which reported lesions of this form of dermatophytid have localized in close proximity to the dermatophytosis on the feet suggests that lymphogenous transfer is a likely manner of dissemination in many cases.

#### SUMMARY AND CONCLUSIONS

Recurrent erysipelas-like lesions on the lower extremities as a complication of dermatophytosis of the feet may be either of bacterial or of fungous origin. In the first instance they are plaques of true erysipelas, the streptococci being transmitted from tinea fissures and erosions by way of the lymphatics. In the second, they are an expression of localized hypersensitivity of the skin to fungous products originating from the focus of dermatophytosis. A case is presented of the latter type, unique because of the localization on the thigh rather than on the usual site of the foot or leg. I share the view that the dermatophytid is an uncommon lesion in comparison with the frequency of bacterial inflammatory manifestations.

The differential features of diagnosis between erysipelas-like dermatophytid and erysipelas are presented. It is emphasized that distinguishing characteristics apply not only to the stage of the active eruption but also to cutaneous sequelae (lymphedema and fibrosis) which are often associated with the bacterial infections and generally not with the dermatophytid, no matter how often repeated. The explanation for these observations is provided by the histopathologic changes, which are predominantly lymphangitic in one and "toxic" (perivascular) in the other. The biologic similarity of the latter to drug eruptions of the fixed type is pointed out.

An immunologic peculiarity in most of the cases in which a fungous allergy is the cause is the atypical response to the intracutaneous injection of trichophytin, exhibited by the immediate development of a wheal. By passive transfer studies, reagin can be demonstrated in the blood serum of these patients. In addition, the typical, or forty-eight hour, reaction usually also appears, but it may be absent or of slight intensity. The immediate reaction to trichophytin injected at the site of the fixed recurrent eruption is intense and spectacular, in keeping with the local "concentration" of tissue hypersensitivity. Here the

<sup>13</sup> Sulzberger, M. B. Personal communication to the author.

<sup>14</sup> Abramowitz, E. W., and Noun, M. H. Fixed Drug Eruptions, *Arch. Dermat. & Syph.* 35: 875-892 (May) 1937.

introduction of trichophytin will reproduce the erysipelas-like exanthem in practically all of its aspects. The development in my patient of an extraordinary flare-up in the same area twelve hours after the subsidence of the immediate reaction is not readily explained, unless it is due, as I have conjectured, to an initial "flash" of the tuberculin type of reaction in highly allergic tissue.

Whichever concept of pathogenesis one favors, the treatment of recurrent erysipelatos phenomena must be directed primarily at suppressing the fungous infection on the feet. The additional measure of intracutaneous injections of trichophytin may enhance the likelihood of preventing recurrences, possibly by inducing specific hyposensitization to the fungous products. It is suggested that the injection of trichophytin directly into the affected area of the skin may provide a more effective means of decreasing the allergic hypersusceptibility.

Commander Marion B. Sulzberger offered valuable advice and kindly criticism.

#### ABSTRACT OF DISCUSSION

COMMANDER M. B. SULZBERGER (MC), USNR. I feel it a privilege to be permitted to open the discussion of this paper, which shows a complete grasp of both the clinical and the immunologic aspects of this subject of recurrent inflammatory swellings of the legs.

Transitory recurrent inflammatory swellings of the legs, with accompanying variable degrees of fever and malaise, are not uncommon. I have seen numerous cases of this kind, not only in clinical and private practice, but particularly in the various surgical and other wards of naval hospitals. In these cases there are no manifest portals of entry on the legs, but often (by no means always) there are open lesions of dermatitis, vesiculation or fissures between the toes or elsewhere on the feet.

Some of these cases fulfil the classic clinical, immunologic and bacteriologic criteria of recurrent erysipelas or cellulitis, but many do not. In the latter group there are cases which present the following evidence in favor of the diagnosis of recurrent erysipelas-like dermatophytid.

- 1 Demonstrable fungi in the lesions on the feet
- 2 No demonstrable pathogenic streptococci
- 3 An urticarial response to trichophytin, accompanied with circulating passive transfer antibodies to trichophytin (most unusual in cases in which the fungi recovered from the feet are not *Trichophyton purpureum*)
- 4 An increased degree of hypersensitivity to trichophytin at or near the site of the lesions on the legs
- 5 Absence of sharp borders, of vesiculation, of supuration and of supervening elephantiasis in the lesions on the legs
- 6 Absence of a local portal of entry on the legs
- 7 Unsatisfactory response to antistreptococcal and other antibacterial medication
- 8 Prevention or reduction of attacks with adequate treatment and prophylaxis of the lesions on the feet

(obviously by far the most important from the practical viewpoint).

These are among the considerations which formed the basis for the concept that in some cases recurrent inflammatory swellings of the legs may be secondary streptococcal or other bacterial eruptions, in others they may be fungus ids, and in still others they may be combined forms. Dr. Waisman's observations lend further support to this concept.

These swellings bear many points of resemblance to the *mumu* swellings of filariasis, and the immunologic responses to trichophytin in cases which I have encountered have their counterparts in the responses to filaria extracts in cases of *mumu*.

In view of this fact the promising results which my colleagues and I have had with trichophytin desensitization in preventing recurrences in some of our cases (*J. A. M. A.* 108:2189 [June 26] 1937) certainly should encourage analogous attempts at desensitization with filaria extracts in *mumu*.

DR. JAMES H. MITCHELL, Chicago. I wish to thank Dr. Waisman for his invitation to help open the discussion of this most interesting paper and to commend him for the excellent, well thought-out investigative work expended on the case he has reported.

My interest in the subject was aroused by the paper of McGlasson, the first of the references in Dr. Waisman's paper read at the Dallas meeting of the American Medical Association in 1926.

In order not to deprive my co-opener of time to discuss the ramifications of allergy involved, I will limit my remarks to the report of a case seen shortly after Dr. McGlasson read his paper and to the projection of a lantern slide of the case.

Before doing so I will quote from the paper of Dr. McGlasson: "It should be remembered that this was before the paper of Ormsby and Mitchell in 1916, and our diagnosis at that time was eczema." Again I quote: "After the paper by Drs. Ormsby and Mitchell, it was possible, except in the case of procaine dermatitis, to find mycelia in practically every case, and the institution of the treatment of eczematoid ringworm resulted in an arrest of the trouble."

A man aged 40 years, a native of Canada and in Chicago on a business trip, was seen Sept. 22, 1927. Four years prior to examination he had bruised his right shin. Later he had a chill, and long-continued fever developed. He completely recovered, but six months later he had a recurrence of the eruption of the shin associated with fever. There were repeated recurrences two or three times yearly. Roentgenogram showed no changes in the bones. Intensive roentgen-ray treatments resulted in a remission for a year and a half. Forty-eight hours before observation another attack occurred. All examinations in Canada had shown nothing abnormal.

From the ankle to the upper margin of the middle third of the right shin the skin was tense, with shiny, palm-sized bluish red areas. The larger areas were on the outer and upper aspect of the leg. The areas were not sharply demarcated, but the outlines were palpable. The temperature was 99.4 F. There were small palpable nodes in the groin. There was an extensive keratotic type of fungous infection of the foot. No fissure, such as might offer a portal of entry for a streptococcal infection, was found in the interspaces of the toes. Microscopic examination disclosed the presence of the organism of the *Monilia* type, but the culture became overgrown with a laboratory tramp and no further opportunity was had for repeating the culture.

The patient was referred to Dr. George Dick at the Presbyterian Hospital, who was actively engaged



investigative work on streptococcic infections at that time. After an intensive examination Dr. Dick reported that there was no evidence of streptococcic infection.

The patient returned home a few days later and was not seen again. It is to be regretted that no further opportunity was had to investigate the case.

My conclusion is that this case may have been an instance of a recurrent erysipelas-like dermatophytid.

DR. S. ROTHMAN, Chicago. I have 3 similar cases in record. All patients had dermatomycosis of the interphalanges of the toes. All displayed hyperkeratoses and rhagades. *Trichophyton gypsum* grew on culture in all 3 cases. All presented the history of numerous attacks of fever over a period of one to three years, recurring about once a month with swelling and redness on the anterior aspect of the lower half of the leg. Lymphedema was present in each case. No streptococci could be recovered from the lesion of the leg. Yet, in spite of the negative bacteriologic results, I strongly believe that these are simply cases of recurring erysipelas which has its portal of infection between the toes. My patients stated that the first few attacks started with violent chills and extremely high temperatures and that the following attacks gradually decreased in intensity simultaneously with a gradual development of lymphedema—in the same manner as it is seen in recurring erysipelas. The cutaneous manifestations were described by the patients as tender red spots which definitely increased in size during the febrile period. One patient stated that the attacks were substantially shortened by sulfonamide therapy.

Demonstration of streptococci in recurring erysipelas may be rather difficult when the temperature is not high and the inflammation is not intense. Whether the patients are carriers of erysipelas streptococci in the rhagades of the toes or whether the organisms are more or less ubiquitous is not known. Possibly a sensitization mechanism plays an important role. But the same problem arises in any case of recurring erysipelas. One should try to culture the streptococci from the rhagades. Unfortunately, we neglected to do this examination.

I agree with Commander Sulzberger that the practitioner should know about this condition. All my patients were under medical treatment and 2 of them were treated with sulfonamide compounds during the attacks, but none of the physicians looked at the patients' toes. No one made an attempt to find the cause of frequent recurrences, and thus the fungous infection remained untreated. In consequence the attacks recurred, and lymphedema resulted. In 1 case even fibrous hyperlasia ("pseudoelephantiasis") developed. Subsequently,

in all 3 cases, mild fungicidal treatment in the clinic completely prevented further attacks. The situation is analogous to that of recurring erysipelas of the face, which can be cured easily by taking care of a chronic rhagadiform lesion in the nares or elsewhere in the face, which represents the portal of infection.

DR. GEORGE M. LEWIS, New York. There is still considerable doubt in my mind regarding the cause of the disorder discussed in this paper. No one has an extensive experience, and in my 2 cases I cultured streptococci as well as fungi and have obtained prolonged remissions from the use of 5 per cent ammoniated mercury ointment, applied to the interdigital webs. The author's thesis that the erysipelas-like lesions are due to fungi is based on clinical, mycologic and immunologic data. The clinical features seem to be at least equally in favor of a pyogenic process. The presence of fungi on the feet is so common that it would have no significance, and the immunologic studies as presented leave one in doubt as to the specificity claimed. Perhaps in the paper as published, there will be demonstrated control tests. If none have been carried out, particularly with staphylococci, streptococci and monovalent vaccines, the increased reactions to trichophyton mentioned by the author may be non-specific and non-significant.

CAPT. MORRIS WAISMAN, M. C., A. U. S. The question raised by Dr. Lewis concerning the specificity of the reaction to trichophyton in this disease was at the first adequately investigated by Commander Sulzberger and his associates. All the evidence points to specific hypersensitivity to trichophyton and permits no doubt of the dermatophytid nature of the lesion. My patient was tested with histamine and staphylococcus toxoid to preclude nonspecific local hyperreactivity, and the degree of reaction to each of these agents was identical on the two thighs. Moreover, a "control" study of a series of patients recovered from cellulitis, retiform lymphangitis and erysipelas on the lower extremities—some of them having recurrent disease—showed distinctly that the affected areas do not react more severely to intradermally injected trichophyton than do the unaffected areas on the opposite extremity. Dr. Rothman is correct in suggesting that streptococci should be demonstrable in fissures between the toes in the cases of recurrent erysipelas or cellulitis on the legs. It was with this thought in mind that I took material for bacterial cultures from the toes of my patient, but these yielded only a growth of nonhemolytic *Staphylococcus aureus* which exhibited no coagulase production indicating a presumptively avirulent strain of organism.

## USE OF SULFATED OIL FOR CLEANSING THE EXTERNAL AUDITORY CANAL

R P LITTLE, M D

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For the cleansing of eczematous skins, dermatologists have found the sulfated oils less irritating than soap because (1) they have a relatively low  $p_H$  and (2) they contain no saturated fatty acids of low molecular weights. Lane and Blank and other investigators have reported satisfactory results from the use of similar detergents. The sulfated oils do not lather, but they clean satisfactorily by virtue of their ability to emulsify and suspend the oils of the skin and various types of external soil. Because of this ability to emulsify other oils and greases, dermatologists use them not only for cleansing per se but for removing ointments from the cutaneous surface.

Eczema of the external auditory canal is similar to eczema of glabrous skin. Patients with eczema of the auditory canal, however, are usually treated by otologists rather than dermatologists. They face the problem not only of cleansing the affected canals without causing further irritation but often of removing cerumen, a greasy material, the removal of which presents the same difficulty as the removal of ointments from the skin. It seemed logical to suppose, therefore, that the sulfated oils might prove helpful in the cleansing of eczematous auditory canals, in the removal of cerumen from the canal and in the prophylaxis and cleansing of infectious eczematoid dermatitis, whose focus is so frequently a furuncle of the canal or an infection of the middle ear or the mastoid antrum or cells.

During the past year a mixture of 25 per cent sulfated vegetable oils, 25 per cent liquid petrolatum and 50 per cent water<sup>1</sup> has been

used as a detergent for general cleansing of auditory canals and especially those which are dry and scaly, with or without a serous exudate. It has also been used in radical cavities where the epidermis is dry and scaly. Since this mixture is water miscible, it can be used equally well on moist and on dry surfaces. After application to a dry surface, it may be washed off with water. It has proved a more satisfactory detergent than alcohol or soap and water and does not cause so much irritation as soap.

Cerumen may be removed with a dull curet but is more often removed by syringing the canal with warm water to which soap or sodium bicarbonate has been added. If the mass is hard it is often softened over a period of a few days by the use of drops of olive oil, hydrogen peroxide or glycerin either alone or with the addition of 4 per cent sodium bicarbonate or with phenol and sodium borate. None of these substances is entirely satisfactory. Olive oil is not miscible with water. Hydrogen peroxide, although it breaks up the mass, may cause pain because of the swelling of the plug. It and the glycerin preparations may cause a dermatitis. The sulfated oil mixture, however, not only softens cerumen and aids in its removal but may be added to the water used in syringing the ear and has the further advantage of not irritating the skin. Its use for cleansing the auditory canal and removing cerumen is suggested as an improvement over the methods generally employed.

147 Avenue B (9)

1 This mixture may be purchased under the name *Acidolate*, from the National Oil Products Company, Harrison, N. J. It is somewhat viscous and may be thinned with water if desired.

# TYROTHRICIN IN CUTANEOUS INFECTIONS

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Since the time of Pasteur, scientists have been interested in the subject of intermicrobial antagonism. A large number of articles on the subject have been written. Waksman and Woodruff<sup>1</sup> divided the group of antagonists so far described into four distinct groups: (1) *Pseudomonas aeruginosa* (*Bacterium pyocyaneum*), *Pseudomonas fluorescens* and related organisms, (2) spore-forming bacteria, (3) actinomycetes (actinomycin), and (4) fungi (penicillin). Dubos,<sup>2</sup> reviewing the subject, dealt with three examples of this type of antagonism—namely, pyocyanase, penicillin and tyrothricin, which he selected because their mode of action is fairly well understood. The object of this paper is to review some of the work done with one of the group, tyrothricin, and to present experiences with the material in the treatment of cutaneous infections up to the present time.

## HISTORICAL

In 1939 Dubos<sup>3</sup> first reported results of his study with a bactericidal substance found in an aerobic spore-bearing bacterium which was later<sup>4</sup> identified as *Bacillus brevis*. This substance, now known as tyrothricin, is the preparation generally used in experimental work because it is more readily available than are its components. Frequently the name "gramicidin" is used synonymously with "tyrothricin." It should be pointed out, however, that both gramicidin and tyrocidine are purified derivatives of the crude extract, tyrothricin.

Hoogerheide<sup>5</sup> prepared a substance from a soil bacillus which was bactericidal for gram-positive organisms and protected mice against lethal doses of pneumococci. This substance apparently is similar to gramicidin.<sup>6</sup>

1 Waksman, S. A., and Woodruff, H. B. The Soil as a Source of Micro-Organisms Antagonistic to Disease-Producing Bacteria, *J. Bact.* **40** 581 (Oct.) 1940.

2 Dubos, R. J. Bacteriostatic and Bactericidal Agents Obtained from Saprophytic Micro-Organisms, *Pediat.* **19** 588 (Nov.) 1941.

3 Dubos, R. J. Bactericidal Effect of an Extract of a Soil Bacillus on Gram-Positive Cocci, *Proc. Soc. Exper. Biol. & Med.* **40** 311 (Feb.) 1939.

4 Dubos, R. J., and Hotchkiss, R. D. The Production of Bactericidal Substances by Aerobic Sporulating Bacteria, *J. Exper. Med.* **73** 629 (May) 1941.

## PREPARATION

In the preparation of the crude substance, staphylococci, pneumococci and group A hemolytic streptococci were added to a special mixture of pooled samples of soil. A small portion of a soil preparation with living cells of a staphylococcus culture was added to a mineral medium. Incubation and a few repetitions of the mentioned process resulted in the isolation of a pure culture of a gram-positive bacillus. After the bacterial cells were allowed to autolyze in an aqueous medium, the lytic agent was obtained in solution. This original substance was found to be bactericidal for many gram-positive organisms, to lyse pneumococci and staphylococci and to inactivate the glucose dehydrogenases of gram-positive cocci,<sup>7</sup> and, in small amounts, to protect mice against infection from pneumococci injected in numbers usually sufficient to kill within seventy-two hours.<sup>8</sup>

Addition of acid acetone to the autolyzed culture produces a water-soluble protein fraction plus an alcohol-soluble, water-insoluble fraction,<sup>9</sup> a grayish powder, which has been named "tyrothricin." The word is derived from Tyrothrix, a generic name indicating sporulating aerobic bacterial species.<sup>10</sup> Treating the water-soluble protein fraction with acid alcohol or

5 Hoogerheide, J. C. An Agent Isolated from a Soil Bacillus Which Inhibits Capsule Formation of Friedlander's Bacterium and Is Highly Bactericidal for Gram-Positive Micro-Organisms, *J. Bact.* **40** 325 (Aug.) 1940.

6 Tishler, M., Stokes, J. L., Tenner, N. R., and Conn, J. B. Some Properties of Gramicidin, *J. Biol. Chem.* **141** 197 (Oct.) 1941. Dubos and Hotchkiss.<sup>4</sup>

7 Dubos, R. J. Studies on a Bactericidal Agent Extracted from a Soil Bacillus. I. Preparation of the Agent, Its Activity in Vitro, *J. Exper. Med.* **70** 1 (July) 1939.

8 Dubos, R. J. Studies on a Bactericidal Agent Extracted from a Soil Bacillus. II. Protective Effect of the Bactericidal Agent Against Experimental Pneumococcus Infections in Mice, *J. Exper. Med.* **70** 11 (July) 1939.

9 Dubos, R. J., and Cattaneo, C. Studies on a Bactericidal Agent Extracted from a Soil Bacillus. III. Preparation and Activity of a Protein-Free Fraction, *J. Exper. Med.* **70** 249 (Sept.) 1939.

10 Hotchkiss, R. D., and Dubos, R. J. Bactericidal Fractions from an Aerobic Sporulating Bacillus, *J. Biol. Chem.* **136** 803 (Dec.) 1940.

acetone yields an inactive precipitate and an active soluble fraction apparently identical with tyrothricin<sup>11</sup> The crystalline substances, gramicidin and tyrocidine, are derived from tyrothricin Gramicidin was so called because of its almost complete specificity for attacking gram-positive organisms<sup>4</sup> Tyrocidine was so named to recall the generic name Tyrothrix and to indicate that the substance is rich in the amino acid tyrosine<sup>4</sup> Stokes and Woodward<sup>12</sup> described a rapid method for developing soil bacteria capable of producing bactericidal agents They plated soil samples in low dilution to obtain many microbial colonies per plate

Two reports<sup>13</sup> showing similar results appeared at the same time on the chemical nature of gramicidin and tyrocidine Hotchkiss and Dubos<sup>14</sup> reported further on the chemical properties of these drugs In the main, they are complex polypeptides

#### TOXICITY

Tyrothricin has proved to be highly toxic by intravenous or intraperitoneal routes, and this will probably limit its use to that of local application Seven of 8 dogs died after daily intravenous injections of 0.4 mg per kilogram of body weight<sup>15</sup> Robinson and Molitor<sup>16</sup> reported that 10 mg given intravenously killed all mice in twenty-four hours, with death apparently due to respiratory failure

The toxicity of tyrothricin is due to its hemolytic effect Gramicidin was first blamed for the hemolysis,<sup>17</sup> and later tyrocidine was shown also

to cause hemolysis<sup>18</sup> Commenting on the difference in observations regarding hemolysis, Mann, Heilman and Herrell<sup>19</sup> stated that when similar tests were made the results depended on the length of time of incubation Tyrocidine caused more rapid hemolysis, but over a period longer than four hours the degree of hemolysis caused by gramicidin was greater

#### MODE OF ACTION

It is known that these substances obtained from soil bacilli are decidedly bactericidal *in vitro* for gram-positive micro-organisms Further, tyrocidine, in the absence of inhibitors in peptone mediums, is also effective against gram-negative organisms<sup>4</sup> The mechanism of its activity is not definite Dubos,<sup>3</sup> observing the inactivation of dehydrogenase (loss of the ability of the cell to reduce methylthionine chloride in the presence of glucose) occurred before any morphologic change could be seen in the bacteria suggested that lysis is only a secondary process occurring after some injury to the cell Later, he<sup>20</sup> proposed that the specificity of gramicidin for gram-positive organisms was possibly due to some unidentified structural difference between gram-positive and gram-negative cells

Gram-positive organisms are susceptible to gramicidin and anionic detergents, but phospholipids inhibit the activity of these compounds This led Miller and co-workers<sup>21</sup> to suggest that possibly the phospholipid content of gram-negative organisms accounts for the inability of gramicidin and anionic detergents to inhibit them

Tyrocidine acts as a protoplasmic poison, causing loss of uptake of oxygen, of production of acid and of reducing ability Gramicidin does not attack these metabolic functions Each has been shown to depress the surface tension of aqueous solutions, tyrocidine more so than gramicidin<sup>22</sup>

11 Hotchkiss, R. D., and Dubos, R. J. The Isolation of Bactericidal Substances from Cultures of *Bacillus Brevis*, *J Biol Chem* **141**:155 (Oct) 1941

12 Stokes, J. L., and Woodward, C. R., Jr. The Isolation of Soil Bacteria That Produce Bactericidal Substances, *J Bact* **41**:33 (Jan) 1941

13 Hotchkiss, R. D. The Chemical Nature of Gramicidin and Tyrocidine, *J Biol Chem* **141** 171 (Oct) 1941 Christensen, H. N., Edwards, R. R., and Piersma, H. D. The Composition of Gramicidin and Tyrocidine, *ibid* **141**:187 (Oct) 1941

14 Hotchkiss, R. D., and Dubos, R. J. Fractionation of the Bactericidal Agent from Cultures of a Soil *Bacillus*, *J Biol Chem* **132** 791 (Feb) 1940, Chemical Properties of Bactericidal Substances Isolated from Cultures of a Soil *Bacillus*, *ibid* **132** 793 (Feb) 1940

15 MacLeod, C. M., Mirick, G. S., and Cuinen, E. C. Toxicity for Dogs of a Bactericidal Substance Derived from a Soil *Bacillus*, *Proc Soc Exper Biol & Med* **43**:461 (March) 1940

16 Robinson, H. J., and Molitor, H. Some Toxicological and Pharmacological Properties of Gramicidin, Tyrocidine and Tyrothricin, *J Pharmacol & Exper Therap* **74** 75 (Jan) 1942

17 (a) Heilman, D., and Herrell, W. E. Hemolytic Effect of Gramicidin, *Proc Soc Exper Biol & Med* **46** 182 (Jan) 1941 (b) Herrell, W. E. and Heilman, D. Experimental and Clinical Studies on Gramicidin, *J Clin Investigation* **20** 583 (Sept) 1941

18 Rammelkamp, C. H., and Weinstein, L. Hemolytic Effect of Tyrothricin, *Proc Soc Exper Biol & Med* **48**:211 (Oct) 1941

19 Mann, F. C., Heilman, D., and Herrell, W. Effect of Serum on Hemolysis by Gramicidin and Tyrocidine, *Proc Soc Exper Biol & Med* **52** 1 (Jan) 1943

20 Dubos, R. J. The Effect of Specific Agents Extracted from Soil Micro-Organisms upon Experimental Bacterial Infections, *Ann Int Med* **13**:2 (May) 1940

21 Miller, B. F., Abrams, R., Dorfman, A., Klein, M. Antibacterial Properties of Protamine Histone, *Science* **96**:428 (Nov 6) 1942

22 Heilman, D. and Herrell, W. E. Mode of Action of Gramicidin, *Proc Soc Exper Biol & Med* **47**:480 (June) 1941

Ferraro,<sup>23</sup> working with eleven strains of *aphylococcus aureus*, found gramicidin more effective than sulfathiazole against these strains. Rammelkamp<sup>24</sup> reported the difference in susceptibility of various strains of *Staph aureus* to the action of tyrothricin. He was able to develop increased resistance in staphylococci by growing them in mediums with increasing concentrations

of tyrothricin

CLINICAL REPORTS ON DERMATOLOGIC DISEASES

Because of the hemolytic activity of tyrothricin, investigators began to use it by local application. An early report by Rammelkamp and Yarefer<sup>25</sup> stated "As far as the evidence goes, it seems clear that superficial infections in man due to staphylococci and streptococci responded in a satisfactory manner following the local application of the material. The dosage and frequency of application requires further study."

Herrell and Heilman<sup>17b</sup> reported good results in treatment of 4 of 8 patients with dermatologic diseases. 1 with ulcer of the leg, 1 with extensive hidrosadenitis suppurativa of the axilla and ulcer of the leg and 2 with eczematoid dermatitis of the hands and feet. However, in a case of dermatitis of the hands and feet, a case of eczematoid dermatitis and in cases of stasis ulcers there was failure to show satisfactory improvement. Later they<sup>26</sup> reported 43 per cent good results, 25 per cent fair results and 32 per cent failure in 50 patients treated, including patients with sinusitis, cystitis, pyemia, infected postoperative wounds, infectious dermatoses and stasis ulcers.

Francis<sup>27</sup> reported clearing a sulfonamide-resistant *Streptococcus pyogenes* infection with gramicidin and following it with a successful skin graft after previous grafts had failed.

Rammelkamp<sup>28</sup> treated 16 ulcers of 12 patients. He obtained satisfactory results when *Staph*

*aureus*, hemolytic streptococci or *Streptococcus faecalis* were present. Twelve of the ulcers became sterile soon after use of tyrothricin was started. Of the other 4, 3 were due to gram-negative organisms and the fourth to a resistant strain of *Staph aureus*. Gram-positive organisms did not respond to tyrothricin when associated with gram-negative organisms, probably owing "to the production of an inhibitory substance by the gram-negative bacteria, since Dubos has observed that the filtrate of cultures of gram-negative bacteria inhibits the action of tyrothricin in vitro."<sup>28</sup> Two patients with eczematous eruptions were also treated. One, whose disease was due to a hemolytic streptococcus, responded.

Wright<sup>29</sup> reported good results for 52 of 57 patients with dermatologic diseases treated, the diseases included cellulitis, diabetic lesions, ulcers of the leg, superficial abscesses, carbuncles, infected cancers and suppurative adenitis.

Kvale, Barker and Herrell<sup>30</sup> concluded that tyrothricin is of definite value in the treatment of ulcers associated with peripheral vascular disease.

L. M. Rankin<sup>31</sup> reported excellent results against five of six chronic ulcers, with good antibacterial response and decided tissue stimulation.

Sergiev,<sup>32</sup> using Gramicidin S (Soviet gramicidin), recorded a recovery time of 41 days for 117 patients with impetigo and 68 days for 23 patients with ecthymic lesions. In 70 per cent of his patients, chronic suppurations of three months to three years' duration were completely healed in sixteen to thirty-one days.

INVESTIGATION OF OINTMENT BASES

Since ointments are so commonly used in the treatment of skin infections, it was decided to incorporate tyrothricin into a variety of ointment bases to test them. Tyrothricin of a strength of 100 mg per hundred cubic centimeters was used. It was believed that this would be a strong enough preparation, since it had been reported in the literature as having been applied in strengths up to 40 mg per hundred cubic centimeters in wet dressings with good results.

The following bases were used as vehicles: (1) petrolatum, (2) hydrous wool fat, (3) rose water ointment, U. S. P., (4) mucilage of tragacanth, U. S. P., (5)

29 Wright, V. W. M. Treatment of Infected Wounds by H-1, a New Germicidal Extract from *St. Bacilli* Cultures, *J. Franklin Inst.* **233** 188 (Feb) 1944.

30 Kvale, W. F., Barker, N. W., and Herrell, V. E. The Use of Tyrothricin in the Treatment of Ulcers of the Extremities Due to Peripheral Vascular Disease, *M. Clin. North America* **28** 849 (July) 1944.

31 Rankin, L. M. The Use of Tyrothricin in the Treatment of Ulcers of the Skin, *Am. J. Surg.* **65** 39 (Sept) 1944.

32 Sergiev, P. G. Clinical Use of Gramicidin, *Lancet* **2** 717 (Dec 2) 1944.

23 Ferraro, W. R. Comparative in Vitro Effects of Gramicidin and Sulfathiazole on *Staphylococcus aureus*, *Bull. New York M. Coll., Flower & Fifth Ave. Hosp.* **5** 164 (Dec) 1942.

24 Rammelkamp, C. H. Observations on Resistance of *Staphylococcus Aureus* to Action of Tyrothricin, *J. Soc. Exper. Biol. & Med.* **49** 346 (March) 1942.

25 Rammelkamp, C. H., and Keefer, C. S. Observations on the Use of "Gramicidin" (Dubos) in the Treatment of Streptococcal and Staphylococcal Infections, *J. Clin. Investigation* **20** 433 (July) 1941.

26 Herrell, W. E., and Heilman, D. Further Experimental and Clinical Studies on Gramicidin, *J. A. M. A.* **118** 1401 (April 18) 1942.

27 Francis, A. E. Sulphonamide-Resistant *Streptococcus* in a Plastic-Surgery Ward, *Lancet* **1** 408 (April 4) 1942.

28 Rammelkamp, C. H. Use of Tyrothricin in the Treatment of Infections, *War Med.* **2** 830 (Sept) 1942.

base consisting of 6 per cent of a group of esters of cholesterol in a petrolatum base<sup>33</sup>, (6) a base containing fatty acid esters of diethenolamine mixed with petrolatum<sup>34</sup> and (7) a base whose formula follows

	Gm or Cc
Cetyl alcohol	15.0
White wax	1.0
Propylene glycol	10.0
Sodium lauryl sulfate	2.0
Water	72.0

Pure cultures of hemolytic streptococci, *Staph aureus* and *Bacillus coli* were obtained and streaked over the surface of the following respective mediums, which had been poured into Petri dishes: hemolytic streptococci on blood agar, *Staph aureus* on plain agar and *B coli* on eosin-methylthionine chloride medium. *B coli* was used as the control because of the inactivity of tyrothricin for this organism. Three-tenths gram of the first ointment was then placed in a compact mass on the surface of the medium of three different plates containing separate organisms as inoculated above. Likewise, 0.3 Gm of the second ointment was placed in a compact mass on the surface of the medium of three different plates containing separate organisms and so on until all seven ointments had been placed in each of three different plates. The plates were then incubated in the usual manner at 37 C and readings taken at the end of twenty-four and forty-eight hours. No inhibition of the growth of any of the organisms was caused by tyrothricin in 100 mg per hundred cubic centimeters strength in any of the ointment bases tested. Colonies grew up to the edge of the ointment mass. It is apparent that the activity of tyrothricin is lost when used in ointment bases so far as the *in vitro* studies to date indicate. These studies were repeated on three different occasions for purpose of confirmation. As controls, 5 per cent sulfathiazole in rose water ointment was tested in the same manner, and this preparation was found to inhibit the growth of staphylococci for 12 mm and of streptococci for 18 mm surrounding the ointment mass.

These experiments, along with poor results from the use of the ointment in 2 cases of impetigo contagiosa, have led to the discontinuance of the use of the drug in ointment bases for clinical purposes until further work is done.

#### OTHER METHODS OF APPLICATION

As another method of application, Rammelkamp<sup>28</sup> applied 95 per cent alcohol containing 50 mg of tyrothricin per cubic centimeter directly to sixteen localized ulcers. This caused a burning sensation at first, which disappeared after two or three applications. After the alcoholic solution dried, sterile dressings were applied. In cases in which exudation from the lesion carried away the tyrothricin with the serum applications were made twice daily. This was especially necessary for ambulatory patients. Good results were obtained in twelve of the sixteen ulcers so treated.

33 This base was Aquaphor, manufactured by the Duke Laboratories, Inc., Stamford, Conn.

34 This base was Hydrosorb, manufactured by the Abbott Laboratories, North Chicago, Ill.

The most popular method for application, tyrothricin has been the continuous wet dressing. The dressing has been impregnated with varying strengths of tyrothricin up to 40 or 100 mg per hundred cubic centimeters. The tyrothricin which is supplied in an alcoholic solution is stable indefinitely at room temperature.<sup>9</sup> Diluting this solution with distilled water results in a milky suspension, although this suspension is stable, it is best to prepare fresh dilutions daily. Isotonic solution of sodium chloride should not be used for diluting because of its tendency to precipitate the active material.<sup>9</sup> As a continuous wet dressing, this suspension is constantly in contact with the lesion and the infecting organisms, a factor which overcomes the inhibitory action of body fluids which precipitate tyrothricin. Rammelkamp<sup>28</sup> "found that serum exudate and feces caused a marked inhibition so that about 100 times the amount of tyrothricin was required to kill streptococci in the absence of these substances was necessary to obtain the same results in their presence."

#### INVESTIGATION OF DILUTED TOPICAL APPLICATIONS

In order to compare the activity of the alcoholic solutions and the aqueous suspensions with that of the ointments, tests similar to those with the ointments were carried out. Freshly prepared dilutions of tyrothricin in 100 mg per hundred cubic centimeters strength were used. The vehicles were (1) 70 per cent alcohol, (2) 50 per cent alcohol, (3) 10 per cent alcohol and (4) distilled water. Three felt pads, 1 cm square were moistened with the first test preparation and placed on the surface of separate Petri dishes on which had been streaked cultures of hemolytic streptococci, *Staph aureus* and *B coli*, respectively. This procedure was repeated for each of the other 3 test preparations. The inhibition of the growth of the micro-organisms

#### *Inhibition of Various Pathogenic Bacteria by Tyrothricin in Solution or Suspension After Incubation for Forty-Eight Hours*

Tyrothricin, 100 Mg/100 Cc	Inhibition (in Millimeters) of		
	Hemolytic Streptococci	Staph Aureus	B Co
70% alcohol	10	8	0
50% alcohol	12	9	0
10% alcohol	7	3	0
Distilled water	6	0	0

recorded in the table. One might assume that 100 per cent alcohol in the alcoholic solutions would cause inhibition of the growth of the organisms, however, this possibility is lessened by the fact that *B coli* was not inhibited even by alcoholic solutions.

As noted in the table definite inhibition of the growth of hemolytic streptococci and *Staph aureus* resulted when they were exposed to solutions or suspensions of tyrothricin. There was no inhibition of the growth of *B coli*. This

states that tyrothricin, which was used in the same strengths in the ointments and the solutions, was inactivated in the ointments, or at least was not released for activity.

#### CLINICAL INVESTIGATION

Twenty patients with cutaneous infections were treated with tyrothricin, included were 4 patients with stasis dermatitis, 6 patients with stasis ulcers, 4 patients with ecthyma, 3 patients with infectious eczematoid dermatitis and 1 patient each with pyoderma, traumatic ulcer and decubitus ulcer. The alcoholic solution (2 per cent tyrothricin in 94 per cent alcohol) supplied was diluted with distilled water to make varying concentrations of tyrothricin in suspension from 40 to 200 mg per hundred cubic centimeters. This suspension was then used in continuous wet dressings. No toxic effects of any kind, either systemic or local, were noted in any patient.

**Results** It is well appreciated that these infections, especially stasis dermatitis and ulcer, will respond to ordinary treatment with rest in bed and the usual wet dressings. Thus, impressions as to the value of tyrothricin wet dressings will have to be brought into the picture. It was noted that the purulent material in most of the cases cleared remarkably well, usually within twenty-four hours. The time required for healing is not shortened, hence it appears that tyrothricin does not promote epithelization.

In the group of 20 cases, results were good in 15 (75 per cent), fair in 2 (10 per cent) and poor in 3 (15 per cent). The infection in the cases in which results were classified as fair (case of stasis dermatitis and 1 of stasis ulcer) cleared well under treatment but soon recurred in the 3 patients for whom results were classified as poor, 1 had an underlying osteomyelitis which did not respond to the tyrothricin although the superficial infection cleared, and 1 with a stasis ulcer and 1 with infectious eczematoid dermatitis showed no response.

In the breakdown of the various groups of similar types of infection, it was found that in 4 of 4 cases stasis dermatitis responded well, while the fourth cleared but reinfection soon occurred. In the 6 cases of stasis ulcers, there was good response in 3, in 1 there was the underlying osteomyelitis, in 1 the ulcer cleared but became reinfected, and in 1 there was no response. Because of the frequent recurrences in hypostatic conditions, these results are not encouraging. All of the 4 ecthymatiform lesions responded in a satisfactory manner. In 1 of 3 cases of infectious eczematoid dermatitis there was poor response, possibly because of associated allergic factors. The results are considered excellent for the traumatic ulcer, pyoderma and decubitus ulcer.

Staphylococci were the infecting organisms in the 3 cases in which the results were poor. This is in agreement with reports in the literature stating that staphylococci are more resistant than streptococci to tyrothricin. This is not discouraging, however, since Ferraro's<sup>23</sup> report indicates that staphylococci are less often resistant to tyrothricin than to sulfathiazole. Eight of our patients had had previous therapy with 5 per cent sulfathiazole ointment without responding. In 5 of these patients, the purulent discharge cleared satisfactorily under tyrothricin wet dressings after having failed to respond to sulfathiazole. A brother and sister were admitted to the hospital at the same time, each with pyoderma, the brother was treated with tyrothricin wet dressings, while the sister was treated with sulfathiazole ointment. The results were considered similar. Similar response was also observed in ecthymatiform lesions on both ankles of a boy aged 3, whose right ankle was treated with sulfathiazole ointment and whose left ankle was treated with tyrothricin wet dressings.

A patient with infectious eczematoid dermatitis on both ears was treated with boric acid wet dressings on the right ear and tyrothricin wet dressings on the left ear. The ear treated with tyrothricin responded more rapidly than the ear treated with boric acid.

#### COMMENT

It was found that tyrothricin when applied in the commonly used strengths was inactive in the several different types of ointments tested. Tyrothricin is seemingly a complex molecule, being made up of gramicidin and tyrocidine, both of which are complex polypeptides. A chemical change or combination would easily be possible in tyrothricin when one recalls the high combining capacity of proteins. Perhaps in suspension in high concentrations it can be used in ointment form.

Because of its complex protein nature, it will probably be impossible to synthesize tyrothricin. This will be a major factor in its availability and cost. If it must be obtained through tedious culture processes, the supply will be limited and the cost high.

#### SUMMARY

A review of the literature on tyrothricin, a bactericidal substance obtained from an aerobic sporulating bacterium, is presented.

In vitro studies show that minute amounts of the material inhibit the growth of gram-positive micro-organisms. Likewise, small amounts protect experimental animals infected with these bacteria.



## ANDERSON—CUTANEOUS INFECTIONS

Because of its high toxicity, the usefulness of tyrothricin is limited to local applications

Tyrothricin is ineffective when incorporated into common ointment bases in the usual therapeutic concentrations

Twenty patients with cutaneous infections were treated with tyrothricin used in continuous wet dressings. The results were good in 75 per cent of the cases, fair in 10 per cent and poor in 15 per cent

The purulent infection clears with remarkable rapidity in most of the dermatologic diseases due to gram-positive organisms. Stimulation of granulation tissue is not apparent

Tyrothricin should prove helpful in clearing infections which are resistant to other types of locally applied medicaments or when sensitivity of the patient to sulfonamide compounds is encountered

This investigation was carried out at the City of Detroit Receiving Hospital, Department of Dermatology and Syphilology, under the supervision of Loren S. Shaffer, M.D.

Condensed from a thesis submitted to the graduate council of Wayne University College of Medicine in partial fulfillment of the requirements for the degree of Master of Science in Dermatology and Syphilology

Parke, Davis & Company, Detroit, supplied the tyrothricin used in this study



# OXOPHENARSINE HYDROCHLORIDE IN TREATMENT OF LUPUS ERYTHEMATOSUS

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For many years the most valuable drugs in the treatment of lupus erythematosus<sup>1</sup> have been salicyl and bismuth preparations. In cases of obstinate lupus erythematosus which does not respond to these conventional drugs and against which sundry methods have been used without success, any remedy which might improve the situation, if only partially, is valuable. This is particularly true if the remedy is a comparatively nontoxic drug.

The organic arsenicals have long had a useful place in the treatment of lupus erythematosus. Neoarsphenamine, the silver arsphenamines, arsotarsons and bismarsen have been used, with some favorable results reported for each. These results made it seem worth while to test oxophenarsine hydrochloride, the arsenical having the best therapeutic index for syphilis, in the therapy of resistant lupus erythematosus.

In July 1942, Dr. M. B. Sulzberger first employed oxophenarsine hydrochloride in a case<sup>2</sup> of widespread chronic discoid lupus erythematosus of long standing, in which all of the conventional methods had been used without success. With the third injection (a total of 30 mg of the drug), there was distinct improvement, the most impressive which had ever been obtained in this case, and many of the lesions are even now much improved. However, after considerable progress no further benefit could be noted, despite continued administration of oxophenarsine hydrochloride.

Encouraged by the results in this case, I used oxophenarsine hydrochloride in the treatment of 20 patients with lupus erythematosus at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. This article reports the first 20 cases.

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<sup>1</sup> Unless otherwise specified, lupus erythematosus refers to the chronic discoid form only.

<sup>2</sup> Baer, R. L. Lupus Erythematosus Disseminatus (treated with Mapharsen), Arch. Dermat. & Syph. 151 (Feb.) 1944.

No auxiliary measures were taken, apart from the use of a plain shake lotion or boric acid ointment, the avoidance of exposure to sunlight and the application of a phenyl salicylate-tannic acid sun-protective solution during the summer months.

For all patients the following investigations were performed before treatment with oxophenarsine hydrochloride was started. Examination of the urine for albumin and sugar, blood cell counts (red, white and differential) and a Wassermann test of the blood. For some patients, particularly those for whom the diagnosis was not clinically established by at least two of the dermatologists of the staff of the Skin and Cancer Unit, a biopsy was performed. When a history suggested the existence of a constitutional disease the possibility was investigated. Treatment with oxophenarsine hydrochloride was not given if there was albuminuria, the white blood cell count was below 4,000 per cubic millimeter, the Wassermann reaction of the blood was positive or the general health was not satisfactory.

The initial dose of oxophenarsine hydrochloride was 5 mg, administered intravenously. Weekly injections were given and the dose was increased by 5 mg each week until a maximum dose of 60 mg was reached in some of the earlier cases. However, it appeared that 60 mg was too large a maximum dose. Mild reactions were frequent enough to warrant reduction of the dose, when it was maintained at 30 mg or less for women and 40 mg or less for men, even mild reactions were rare and improvement, when it occurred, was usually continued.

In some cases distinct improvement was noticeable even after the second or third injection, but in others no change was seen until the sixteenth or eighteenth dose, when a sudden and dramatic improvement was observed. Treatment was discontinued when a total of 1,200 mg of the drug had been administered if no clinically distinct improvement had taken place. When 1,200 mg had been administered, a rest of four to six weeks was allowed before a second course was started for patients whose condition warranted a continuance.

When injections were given at intervals of more than one week, fresh lesions would sometimes develop. After treatment was ended on account of apparent cure, there were recurrences in some cases. Administration of the drug was resumed in these cases but it is too early to judge its effects on such recurrences.

In only 1 case (case 20) was it found necessary to discontinue use of oxophenarsine hydrochloride because of its toxic effects. In some cases there was little or no improvement, as was to be expected in cases of disease whose cause is entirely unknown.

*Review of Twenty Cases of Lupus Erythematosus Treated with Oxophenarsine Hydrochloride*

Case	Sex	Age, Yr	Duration of Disease, Yr	Latent	Treatment Previously Given	Injections, Number	Result	Comment
1	F	17	28	Right lower conjunctival margin, lips and chin	"Acid", 327 injections of gold and 9 injections of bismuth	40	Good	Conjunctival lesion responded
2	F	49	20	Right lower conjunctival margin, chin and cheeks	40 injections of bismuth, 36 injections of gold, sobisminol	16	Excellent	Conjunctival lesion responded
3	F	58	3/4	Nose, temples and cheeks	None	40	Good	
4	M	53	1/2	Face, ears, forehead and sternum	None	26	Excellent	See case history 4 and figures 1, 2, 3 and 4
5	M	48	9	Cheeks	25 injections of bismuth, 10 injections of gold	36	Good	
6	M	37	Many	Cheeks	None	17	Good	
7	M	33	Many	Nose	10 injections of bismuth	22	Good	
8	M	53	17	Most of face, forehead and chest	40 roentgen treatments, 20 injections of bismuth, 30 injections of gold	35	Excellent	Rapid response after third injection of oxophenarsine hydrochloride; permanent radiodermatitis
9	F	30	10	Cheeks and left eyebrow	22 injections of bismuth, 31 injections of gold	16	Good	
10	M	51	27	Most of face	"Acid", solid carbon dioxide, 1 year of roentgen treatments, many ultraviolet irradiations, 2 applications of radium, 6 months' treatment with gold, 6 months' treatment with bismuth, removal of epithelioma by diathermy	40	Unsatisfactory	Considerable radiodermatitis, numerous keratotic nodules
11	F	54	Unknown	Cheeks	None	11	Excellent	
12	F	35	1	Cheeks and temples	12 injections of gold, 22 injections of bismuth	40	Good	
13	F	41	Many	Vertex	40 injections of bismuth	31	Unsatisfactory	Subsequently responded excellently to one application of solid carbon dioxide
14	M	55	3 1/2	Nose	3 injections of mercuric salicyl arsenate, 31 injections of bismuth, 71 injections of gold	30	Good	
15	F	43	5	Chin and cheeks	22 injections of bismuth, 31 injections of gold, solid carbon dioxide, 6 ultraviolet irradiations	30	Unsatisfactory	
16	M	49	2 1/2	Cheeks and temples	22 injections of bismuth, 20 injections of gold, 6 roentgen irradiations	29	Excellent	See case history 16 and figures 5 and 6
17	M	39	2 1/2	Forehead and neck	2 injections of bismuth, 21 injections of gold	21	Excellent	Bismuth was discontinued on account of abdominal pain after injection
18	M	27	1 1/2	Ears, nose and cheeks	12 injections of gold, 31 injections of bismuth	32	Unsatisfactory	
19	M	52	21	Nose and cheeks	26 applications of radium, 18 injections of triphal 6 injections of bismuth	12	Unsatisfactory	Considerable radiodermatitis and atrophy
20	F	47	12	Nose, chin and upper lip	100 injections of gold	15	Unsatisfactory	Oxophenarsine hydrochloride had to be discontinued because of edema of the eyelids after injection

Lupus erythematosus of the mucosae is notoriously resistant to therapy, and, as far as the buccal mucosa was concerned, no decided changes were seen with oxophenarsine hydrochloride, although improvement sometimes occurred. When, however, the disease involves the

been eminently satisfactory and arrest of activity seems complete and so far permanent.

The term "cure" is an unsafe one to use when speaking of lupus erythematosus, and only time can tell whether, though one lesion of lupus

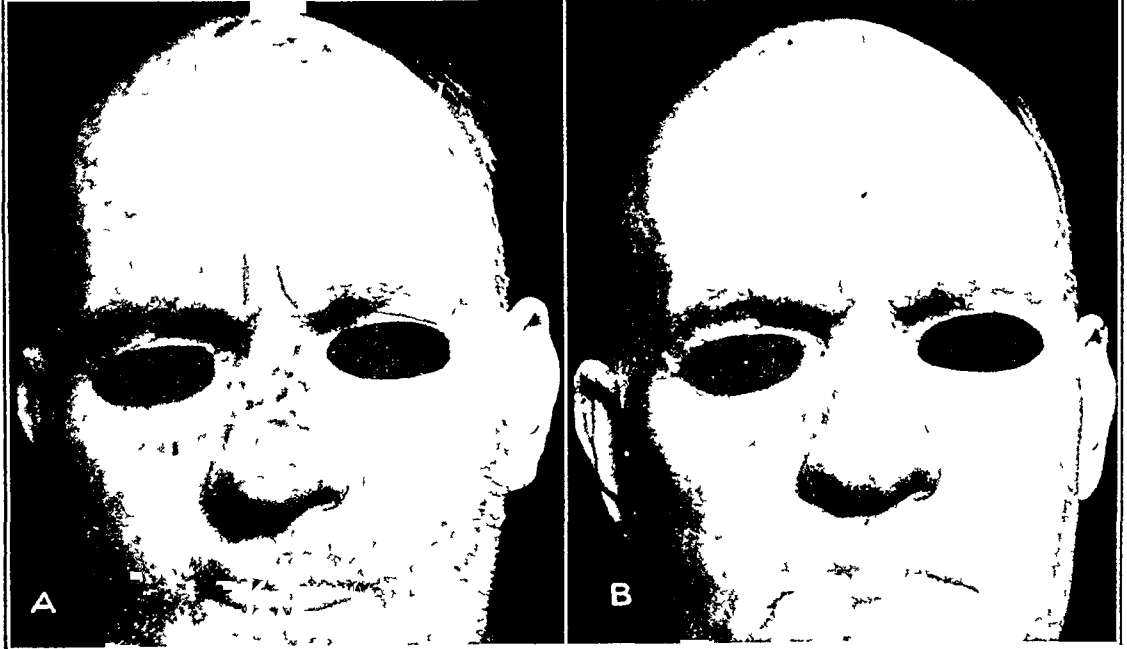


Fig 1 (case 4) —A, lupus erythematosus before treatment with oxophenarsine hydrochloride, January 1942. B, results of treatment with oxophenarsine hydrochloride after six months of use, July 1942.

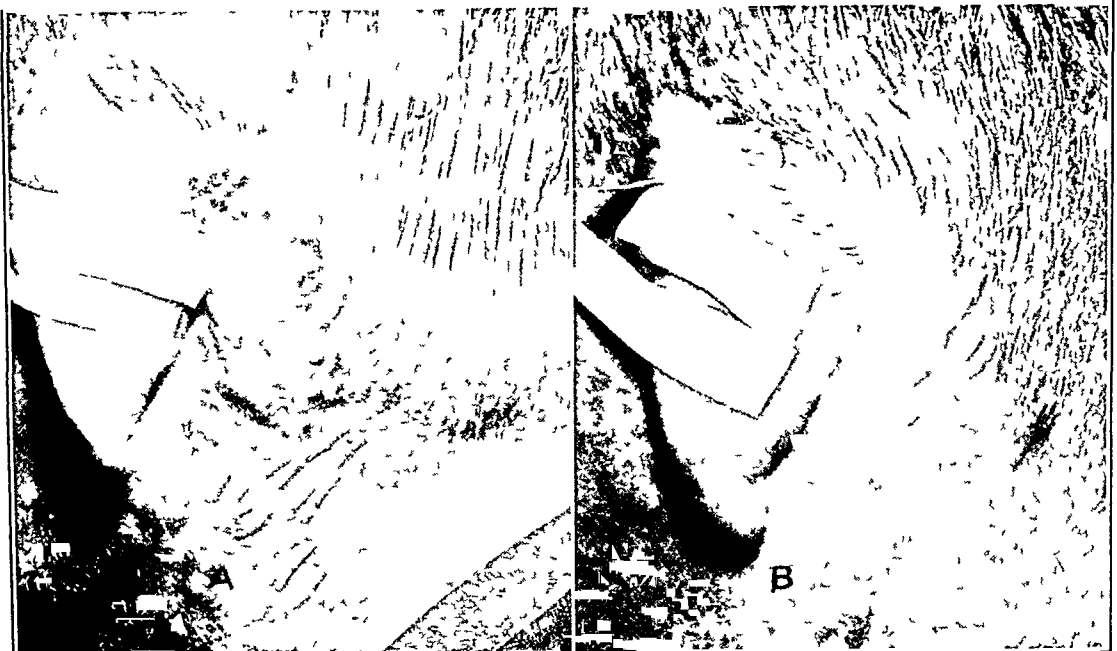


Fig 2 (case 4) —A, lupus erythematosus before treatment with oxophenarsine hydrochloride, January 1942. B, results of treatment with oxophenarsine hydrochloride after six months of use, July 1942.

pebral conjunctiva, it is probably a valuable drug and cases have been observed in which, though the conjunctival lesions have proved resistant to all other methods of treatment, response to oxophenarsine hydrochloride has

erythematosus is apparently cured, another may not appear either on the same site or on a different area. It would therefore be more accurate to speak of the "arrest" of lupus erythematosus rather than of its "cure."

## LUPUS ERYTHEMATOSUS

With this in mind, it may be said that in a certain proportion of cases of lupus erythematosus oxophenarsine hydrochloride will arrest the disease and that it is an effective drug, worthy of trial in cases in which the disease is refractory to bismuth and gold therapy. Prolonged observation will be needed before one can advise it as a therapeutic substance to be adopted in preference to heavy metals. From the syphilologist's vast experience, it is apparent that oxophenarsine hydrochloride is a safer drug than a gold preparation.

sive treatment with bismuth and gold preparations, among the 4, 1 had permanent and severe radiodermatitis. In this case (case 8) response of the lupus erythematosus to oxophenarsine hydrochloride was rapid. In 8 other cases improvement was shown, but no complete "cure." In 6 of them courses of bismuth and gold preparations had previously been given. In 1 (case 2) the conjunctival lesion, which had been present for three years, in spite of treatment, cleared with administration.



Fig 3 (case 16) —Lupus erythematosus before treatment with oxophenarsine hydrochloride, January 1943

ation, though more liable to have unpleasant associated effects than one of bismuth.

One should hesitate to use oxophenarsine hydrochloride for the acute and more active subacute types of lupus erythematosus until much greater experience has been acquired, no such types have been included in the series treated so far.

### COMMENT

Oxophenarsine hydrochloride produced excellent results in 6 of the 20 cases in this series. The patients 4 had previously received extensive

of oxophenarsine hydrochloride. This drug gave unsatisfactory results in 6 cases, in all of which prolonged treatment with bismuth and gold compounds had previously been given. Two of the patients (cases 10 and 19) were suffering from severe radiodermatitic changes when treatment with oxophenarsine hydrochloride was begun. 1 patient (case 20), the only one in the series, had to discontinue treatment with the drug on account of edema of the eyelids, and 1 patient (case 13) who was totally unresponsive to oxophenarsine hydrochloride was "cured" by one application of solid carbon dioxide.

REPORT OF CASES

The following case is an example of early response to oxophenarsine hydrochloride when no previous treatment had been given

CASE 4—C H, a 53 year old man, first attended Skin and Cancer Unit of the New York Postgraduate Medical School and Hospital on Jan 29, 1942. He gave an unreliable history of lesions on the face six months. He had extensive lesions of typical lupus erythematosus on the flush area of the face, around the ears and on the forehead and sternum. Administration of oxophenarsine hydrochloride was started on February 5, and definite paling occurred

cold patches of erythema, scaling, atrophy and alopecia on both sides of the face from the angles of the mandible to the temples and left frontal area of the scalp. Administration of oxophenarsine hydrochloride was started, and by the twelfth injection improvement was definite. By the twenty-ninth injection no evidence of disease remained other than pale smooth depressed areas of alopecia. The result was most satisfactory.

SUMMARY AND CONCLUSIONS

Oxophenarsine hydrochloride was used in the treatment of lupus erythematosus in 20 cases. The average duration of the disease was nine



Case 4 (case 16) —Results of treatment with oxophenarsine hydrochloride after eight months of use, September 1942. Within one week. By July 27 all lesions showed dramatic improvement and little remained beyond atrophy of the affected sites. The patient had received a total of twenty-six injections (1,120 mg) with an excellent result.

The next case shows the value of this drug for patients who had previously been given much treatment with heavy metal without success.

CASE 16—S C, a man aged 49, was first seen at Skin and Cancer Unit of the New York Postgraduate Medical School and Hospital on Jan 4, 1943. He gave a history of lesions on the face for two and one-half years, for which he had received twenty-two injections of bismuth preparation, twenty of gold preparation, and six roentgen treatments. He showed dis-

seminated patches of erythema, scaling, atrophy and alopecia on both sides of the face from the angles of the mandible to the temples and left frontal area of the scalp.

Results noted were excellent in 6 cases, good in 8 and unsatisfactory in 6. There were no serious ill effects.

The drug may be used in treatment of lupus erythematosus with a fair expectation of success, even in cases in which the disease has resisted all forms of treatment commonly in use.

A long period of observation is necessary for the evaluation of oxophenarsine hydrochloride in the treatment of lupus erythematosus.

2 West Eighty-Seventh Street

# LOCALIZED SENSITIVITY TO CRUDE PENICILLIN

## REPORT OF A CASE

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In October 1943 Robinson and Wallace<sup>1</sup> reported on the use of penicillin-inoculated gauze pads for topical application in the treatment of various superficial infections. Since that time there has been considerable use of crude penicillin in compresses and in ointment bases for the treatment of superficial pyogenic dermatologic diseases. In a recent discussion one investigator,<sup>2</sup> reporting encouraging results from the treatment of acute and of chronic pyogenic infections of the skin, stated "Up to the present there has been no serious reaction reported following the local or parenteral use of penicillin.

Its absence of local reaction and sensitivity places the mold in a unique situation in comparison with the sulfonamide compounds."

Evidence is accumulating, however, to indicate that the use of penicillin locally is not wholly unattended with untoward responses. In July 1944 a case of dermatitis venenata of the face and genitalia from contact with purified penicillin was reported.<sup>3</sup> The patient was a medical officer who prepared various solutions of purified penicillin and administered the drug to patients. A strongly positive reaction to a patch test was obtained in that patient. Raper and Coghill<sup>4</sup> recently stressed the possibility of sensitization to mold protein, which inevitably is present in such preparations.

In this clinic, crude penicillin applied locally has yielded good results in the treatment of cutaneous infections. However, in some patients the dermatitis has become worse after such therapy. Three patients seemed irritated by this preparation as soon as it was applied. This irritation was primary, and these persons did

not show a sensitive reaction to patch tests. In another patient pronounced local sensitivity to crude penicillin was encountered. The experience in this case forms the basis of the present report.

## REPORT OF CASE

M. H., a 34 year old housewife, was seen in the dermatologic clinic of the University of Pennsylvania School of Medicine, on Nov 30, 1943, with a circumscribed subacute eczematous dermatitis on the dorsum of the right hand and the adjacent portion of the ring, middle and little fingers. Five and a half years previously the patient had a similar dermatitis on that hand which was resistant to the usual forms of local therapy, and



Fig 1—Original dermatitis on the dorsum of right hand prior to therapy with crude penicillin.

It was thought that a contact factor, plus a highly neurotic element in the home, kept the dermatitis from healing. The patient received roentgen ray therapy and lay down exposures of the hand to artificial sunlight. There were slight improvements and many generalized exacerbations, and on two different occasions the patient was hospitalized. During that period she was found to be sensitive to resorcinol and Castellani's paint, and during both hospitalizations rather large doses of one of the sulfonamide compounds were used to control and eventually to clear the dermatitis. The patient had been well for a few months when the dermatitis recurred. She was hospitalized for several months in another institution where she received considerable roentgen

On leave of absence from the Department of Dermatology and Syphilology, University of Pennsylvania School of Medicine, Dr John H Stokes, Director

1 Robinson, G. H., and Wallace, J. E. Inoculated Penicillin Dressings, *Science* 98:329 (Oct 8) 1943

2 Johnson, H. M. Penicillin Therapy of Impetigo Contagiosa and Allied Diseases, *Arch Dermat & Syph* 50:1 (July) 1944

3 Pyle, H. D. and Rattner, H. Contact Dermatitis from Penicillin, *J. A. M. A.* 125:903 (July 29) 1944

4 Raper, K. B., and Coghill, R. D. "Home Made Penicillin," *J. A. M. A.* 123:1135 (Dec 25) 1943

rapy and eventually became well. The skin remained clear for almost two years, but the dermatitis recurred in the later months of 1943.

On Jan. 10, 1944, because the localized patch on the back of the right hand had not responded to treatment, incisions were made from the lesion, and many hemolytic and nonhemolytic staphylococci and nonhemolytic streptococci were found. Crude penicillin was given to the patient to be used in the form of compresses and ointment form (the ointment was 50 per cent crude penicillin in Lanette wax base). In one week the dermatitis was much improved. The pruritus had stopped, the lesion was dry, and there was some central healing. Treatment was continued, and a week later, although there was central healing, there seemed to be slight peripheral spread. The patient was seen on that day by another physician, who prescribed 5 per cent distillate ointment. A week later the patient remained much worse, and at this time, February 1, crude penicillin was again given. In one week the dermatitis was again much improved. There was some central clearing, and normal skin could be seen. At the end of

the arms and face. There was less involvement on the trunk, and a generalized pruritus was present. The patient responded to compresses of acriflavine and potassium permanganate solutions and boric acid ointment. This treatment was carried out in the home, and the entire process subsided, leaving the original localized dermatitis on the dorsum of the right hand.

On March 10, 1944, crude penicillin ointment was again tried, and the patient returned in three days with an extremely acute dermatitis on the original focus. This was followed by an extension of the dermatitis up the forearm and an id type of reaction, which was much more severe and generalized than the previous one, and the patient had to be hospitalized. A generalized papular eruption had developed, with acute eczematous dermatitis affecting both hands and forearms. The patient responded favorably to hospital treatment, and her skin was clear within two months. The patch of dermatitis on the dorsum of the right hand had likewise almost completely subsided.

#### ALLERGIC STUDIES

It was believed that this patient was sensitive to crude penicillin, and investigations were accordingly carried out.

The crude penicillin was prepared by Albert Kelner, Ph.D., Research Fellow<sup>5</sup> in the William Pepper Laboratory of Clinical Medicine. *Penicillium notatum*, strain 1249 B 21, was grown undisturbed at room temperature in a modified Czapek-Dox broth containing 4 per cent dextrose and 1 per cent Difco yeast extract. After seven to nine days the crude penicillin was harvested by decanting the medium from the mycelial mat. Some spores and a few mycelial shreds remained in the harvested material. The pH was adjusted with monobasic potassium phosphate from the initial value of 7.7 to 7.9 to about 6.5. The crude penicillin inhibited *Staphylococcus aureus* in dilutions of 1:500 to 1:1,000. The mycelial mats were examined carefully for the presence of contaminants. As a further check for bacterial contamination, deemed sufficient for the purposes of this study, dilutions of the adjusted harvested material were made in nutrient broth tubes, which were observed for the development of turbidity after incubation at 37°C. for seven days.

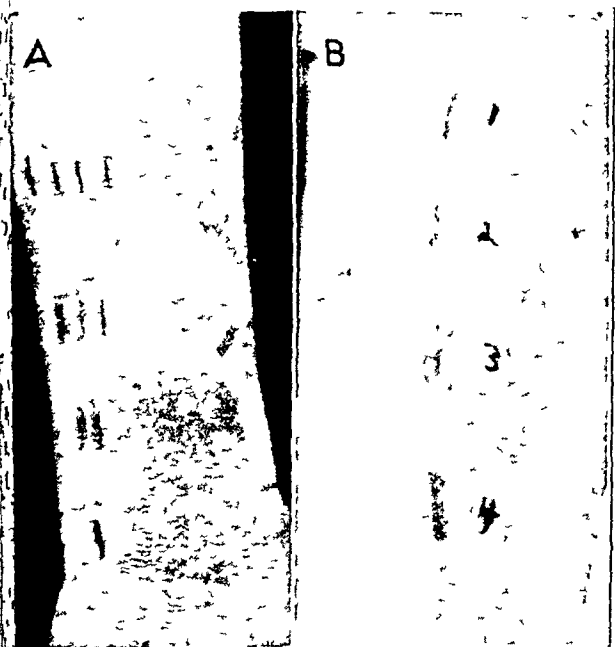


Fig. 2—A, patch tests on the dorsum of right wrist and forearm just above the original dermatitis, demonstrating sensitivity to crude penicillin. The material used at each site was (1) crude penicillin, (2) crude penicillin and Lanette wax ointment base, (3) the culture broth on which the penicillin was grown (control), (4) the Lanette wax ointment base (control). The testing material was removed and the photograph taken forty-eight hours after the patches were applied. B, scratch tests demonstrating sensitivity to crude penicillin. The material used at each site was (1) culture broth on which the penicillin was grown, (2) the ointment base, (3) crude penicillin and (4) crude penicillin in the ointment base. The photograph was taken twenty minutes after the scratch tests were made.

the next week there was further clearing, but there was a peripheral extension of the dermatitis in the form of small red papules. When seen seven days later, the dermatitis was much worse. There was beginning extension of the dermatitis up the right forearm, and within two weeks a similar dermatitis had developed on the dorsum of the opposite hand. This was followed quickly by the development of small papular erythematous lesions on

On May 23 closed patch tests with crude penicillin ointment, the culture fluid for the growth of penicillin and the ointment base (Lanette wax) were applied on the dorsum of the right hand and wrist just above the site of the original localized dermatitis. In forty-eight hours the patch tests were read. The crude penicillin alone and in the ointment form elicited strongly positive reactions with a pronounced erythema and vesiculation. The reactions to control tests with the culture fluid and ointment base were entirely negative. Patch and scratch tests to purified penicillin elicited negative reactions. Reactions to scratch tests with crude penicillin on the forearm were positive. A less positive reaction to ointment and negative reactions to scratch tests with the controls were obtained.

5 Supported by Smith, Kline and French Antibiotic Research Fund.

Patch tests with penicillin applied to the back of the opposite arm and hand elicited negative reactions (crude penicillin had not been used therapeutically on the left hand). The results of the same patch tests when applied to the dorsum of the right hand were repeatedly positive. A patch test on the right forearm gave a doubtful reaction, and a series of patch tests to this material on the dorsum of the right hand and forearm further proved the patient to be only locally sensitive, as the testing material elicited positive reactions on the dorsum of the hand and completely negative reactions high on the forearm. Passive transfer tests with blister fluid from the opposite arm and later from the original dermatitic area were attempted for this patient. The reactions to the former tests were completely negative, and the reactions to the latter suggested a positive transfer of antibodies.

Patch tests with the crude penicillin preparation and the control material were made in 50 normal patients. Some of these patients had received purified penicillin by intramuscular injections, others had used crude penicillin locally while the rest had never been in contact with any of the testing materials. None of the patients had positive reactions to any of the testing materials.

#### SUMMARY AND CONCLUSION

A case of localized sensitivity to crude penicillin was observed, and special allergy studies were made.

Although crude penicillin is effective in treating certain types of superficial pyogenic cutaneous infections, occasional local reactions with the development of sensitivity may be expected.



# TREATMENT OF DERMATOPHYTOSIS AND HYPERHIDROSIS WITH FORMALDEHYDE AND CUPRIC SULFATE IONTOPHORESIS

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Because of the large numbers of persons affected, dermatophytosis remains an important therapeutic problem in military and civilian life. It has been well said that the conditions favoring the perpetuation of the infection are heat, moisture and darkness of the leather-shod foot. The failure of most therapeutic procedures in treating ambulatory patients is due to the continuance of these conditions during the course of therapy.

It was thought possible that if any one of the three factors which perpetuate the infection, heat, moisture and darkness were eliminated, fungi could no longer survive. Most attempts at controlling moisture have been based on the use of foot powders which absorb the moisture after it has reached the surface. The course of treatment proposed herein utilizes the principle that sweat formation is inhibited at its source, thus producing a drier epidermis in with any other known method.

This effect is produced by the use of 1 per cent solution of formaldehyde given by the method of iontophoresis. This method was used by Pinson<sup>1</sup> in studying insensible heat loss in the absence of sweating. He demonstrated that after two to three administrations of formaldehyde by iontophoresis the activity of the sweat glands in the area treated is completely inhibited for a period of approximately one month.

It is further well established that solution of formaldehyde is an excellent fungicide. It has been used for many years in the disinfection of shoes and in the treatment of dermatophytosis. However, application of fungicidal agents to the surface of the skin should not be as effective as iontophoresis, since this method causes migration of the fungicide through the deeper layers of the epidermis.

That iontophoresis does not result in systemic absorption is indicated by the fact that medicinal drugs as a rule cannot be made to migrate far below the surface of the skin, consequently, local medication is essentially a local or intra-

dermal form of treatment and systemic effects are an exception.<sup>2</sup>

In recent years there have been favorable reports concerning the use of cupric sulfate by iontophoresis in the treatment of dermatophytosis.<sup>3</sup> A dissenting opinion concerning its use has been expressed by Greenwood and Rockwood,<sup>4</sup> who have stated that the method must be ineffective since cultures positive for dermatophytes were obtained after a series of treatments with the copper solution. Their experience was based on a series of only 4 cases. Furthermore, the question of positive cultures is largely academic, since fungi can be cultured from normal skin and since the knowledge of the etiologic factors involved in the pathogenesis of dermatophytosis is so deficient. In this study I was interested more in actual therapeutic results than in theoretic questions of fungicidal activity.

## METHOD

Figure 1 is a diagram of a simple electrical circuit for administering a current of low milliamperage. A rheostat is used in series with a 45 volt dry cell battery and a milliammeter with a scale reading from 1 to 30 milliamperes. The negative lead is connected to a lead plate which is covered by gauze soaked in saline solution, on which the patient places the palm of his hand. The positive lead is connected by means of a small piece of copper foil to a porcelain pan containing either 1 per cent formaldehyde or a 1 per cent cupric sulfate solution. The patient soaks his feet in the formaldehyde bath with his hand on the gauze-

2 Kovacs, R. *Electrotherapy and Light Therapy*, ed 4, Philadelphia, Lea & Febiger, 1942, p 155.

3 Jersild, O., and Plesner, M. *Traitement de l'epidermophytie des extremités par iontophorese de cuivre*, Bull Soc franç de dermat et syph **43** 450 (Feb) 1936. Haggard, H W., Strauss, M J., and Greenberg, L A. *Fungous Infections of the Hands and Feet Treated by Iontophoresis of Copper*, J A M A **112** 1229 (April 1) 1939. Gunderson, G O. *Copper by Iontophoresis in Treatment of Dermatophytosis*, Indust Med **9** 405 (Aug) 1940. Solomon, W M. *Treatment of Dermatophytosis by Ion Transfer*, Arch Phys Therapy **23** 214 (April) 1942. Glauser, F. *Management of Fungus Infection of the Feet*, U S Nav M Bull **43** 525 (Sept) 1944.

4 Greenwood, A M., and Rockwood, E M. *Iontophoresis (Ion Transfer) of Copper Sulfate in Cases of Proved Infection*, Arch Dermat & Syph **44** 800 (Nov) 1941.

1 Pinson, E A. *Evaporation from Human Skin and Sweat Glands Inactivated*, Am J Physiol **137** (Oct) 1942.

covered lead plate for twenty minutes, the rheostat being adjusted to a current of 10 to 12 milliamperes (fig 2). Little discomfort is produced by this method.

The diagnosis of dermatophytosis was made as carefully as possible on clinical grounds. It is realized that some mistakes in diagnosis may have been made. Those patients who had mild infections were given two or three treatments with formaldehyde on successive days, while those with severe infections were given three to four treatments on alternating days. More treatments were required when cupric sulfate was used. Cracked and macerated areas between the toes were protected between treatments by inserting loose pledgets of ab-

keratin layer over the diseased portions. Denudation might occur as a result of the rubbing against each other in walking. The protection was readily achieved by instructing the patient to keep the involved toes separate with pledgets of absorbent cotton during the treatment.

Formaldehyde by iontophoresis, however, was less satisfactory than cupric sulfate in the treatment of severe lesions exhibiting extensive denudation. Formaldehyde was too caustic in open lesions, causing pain and an inflammatory reaction. Although a greater number of treatments were required with cupric sulfate, it caused little pain or inflammation and was therefore better tolerated by the patient. It also proved adaptable in cases of severe infection to treat secondary infection for the first two or three

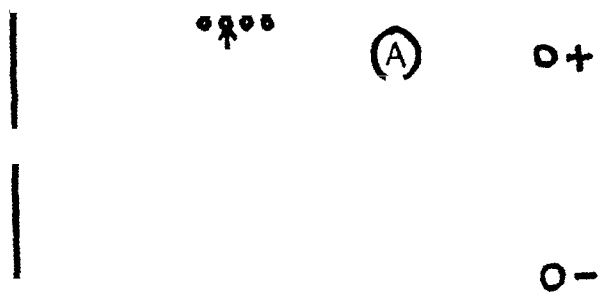


Fig 1—Diagram of electrical circuit

sorbent cotton between the affected toes. Denuded, secondarily infected areas were treated with a 5 per cent sulfathiazole ointment applied after the administration of iontophoresis. The ointment was used only for short periods in order to avoid the danger of sensitization reactions to sulfathiazole. Plain petrolatum was used on areas of skin which cracked because of excessive dryness. The patient was instructed not to apply this on treatment days, as this interfered with the passage of the iontophoretic current.

#### RESULTS

The table summarizes the results of treatment. The data are necessarily approximate, since it proved impossible to judge the exact day that "clinical improvement" and "clinical remission" occurred.

While formaldehyde and cupric sulfate by iontophoresis were both found to be extremely effective in the treatment of the superficial mycoses, each proved to have its own field of usefulness.

Formaldehyde was most effective in cases of uncomplicated hyperhidrosis and of dermatophytosis of moderate severity. The suppression of the sweat glands was, of course, not permanent, the effect lasting about three to four weeks, but the tremendous relief afforded the patient warranted repeated therapy during the hot weather.

Patients with moderate dermatophytosis required about three daily treatments to effect a remission. The lesions usually cleared without further therapy in a period of approximately two weeks following the last treatment. When lesions were on the sides or webs of the toes it was necessary to protect these areas until healing occurred because formaldehyde iontophoresis resulted in desquamation of the



Fig 2—The apparatus in use

days with applications of hot compresses, lance the purulent vesicles and use of sulfadiazole by mouth (1 Gm three times a day) before iontophoresis was begun.

The cupric sulfate solution was also used successfully for the occasional patient who complained of severe pruritus following the use of formaldehyde and for 2 who did not respond to formaldehyde. There were, similarly, 3 patients not responding to copper sulfate who had lesions cleared with the use of formaldehyde. Two patients for whom the diagnosis of fungal infection was doubtful resisted both forms of therapy.

Patients exhibiting severe chronic eczematous lesions with phytid reactions on the ankles



Fig 3—Hands and feet before treatment



4—The same hands and feet one month later, after three treatments with solution of formaldehyde

and hands who had been therapeutic problems under routine care responded to one or the other solution. The number of treatments in this group varied from five to seven with formaldehyde, but the resolution was more rapid (figs 3 and 4).

The group with severe phytid reactions on the hands responded so well that they deserve special mention. Most of these patients had been under treatment for months without improvement. The results appeared to be as good as with irradiation therapy, without the dangers of the latter form of treatment. In some of these cases the diagnosis was doubtful because no active lesions on the feet could be demonstrated, but in these cases there was as good a response as in the cases of active infection of the feet.

For the group with phytid reactions, considerable caution should be exercised in treat-

## COMMENT

It is doubtful that iontophoresis acts by fungicidal activity alone, since phytid reactions on the hands respond as well as active dermatophytosis of the feet does. Iontophoretic treatment to the feet alone does not cause the disappearance of the phytid reactions of the hands as quickly as treatment to both hands and feet does. On the other hand, treatment of the hands alone will ameliorate the phytid reaction of the hands without affecting the lesions on the feet. The mode of action of iontophoresis is, therefore, unknown, except that it causes desquamation of the keratin layer over the diseased portions and leads to relative complete cessation of sweating.

Cupric sulfate is said to be a weak fungicide against those fungi found in association with dermatophytosis.<sup>4</sup> Formaldehyde is fairly

## Results of Treatment

Severity of Disease	Number of Cases	Average Number of Treatments	Average Time to Clinical Improvement, Days	Average Time to Clinical Remission, Days	Average Time of Hospitalization	Failures
A With Formaldehyde						
Mild	19	3	2	5		0
Moderate	42	3	2	10		3
Moderately severe	8	3-4	5	20		3
Severe	5	4-7	7	40	20	2
Uncomplicated hyperhidrosis	11	3	1	3		0
B With Cupric Sulfate						
Mild	8	5	3	10		0
Moderate	11	5	3	10		2
Moderately severe	8	7	4	12		1
Severe	6	7-12	4	30	20	2
Uncomplicated hyperhidrosis	2	5	2	6		1

ing the lesions on the feet early. Frequently treatment of the feet has resulted in an exacerbation, usually of minor severity of the phytid lesions elsewhere. I have found that the most efficacious method for ambulatory patients is to treat the phytid reaction for several weeks before treatment of the feet is attempted.

Treatment of the feet at this time will usually result in a minor exacerbation of the eruption on the hands which can be easily managed. Hospitalized patients were given treatment to the hands and feet simultaneously, and the flare-up in the phytid reaction was allowed to run its course in order to shorten the duration of hospitalization. If the exacerbation is severe it is wise to discontinue treatment of the feet for a time. The general principle that over-treatment will result in an exacerbation of the phytid reaction holds for iontophoresis and one should be guided by one's judgment of the clinical response in each case.

Whether or not formaldehyde iontophoresis produces its effects by killing the fungus or by so altering their environment that the continued activity becomes impossible cannot be stated from this study. Further investigation by clinics equipped with laboratories capable of carrying out careful cultural studies is needed.

My object was to find a method for treating dermatophytosis that would return men in the armed forces to full active duty quickly. Although many of the standard methods of therapy are fairly good, their effectiveness depends to a great extent on the ability and conscientiousness of the patient in maintaining a program of constant treatment on himself for several weeks or more. In actual practice many patients in the armed forces will fail to persevere in such rigid care of their feet. They will neglect to wash their feet and apply medications twice each day. For such patients iontophoresis has a definite usefulness since

quires little or no cooperation on the part of the patient.

A further advantage is that after the first one or two treatments the feet are no longer painful and the patient can resume full activity without discomfort. In cases of moderate severity after the feet have become dry, usually after the second or third treatment the patient need be seen only at five or seven day intervals, requiring further therapy if necessary. The healing process continues without attendant care from the patient or physician.

Thus, the question of fungicidal activity was for my purposes largely academic. There is a clinical entity diagnosed by clinicians everywhere as "athlete's foot." Iontophoresis of solution of formaldehyde or cupric sulfate is effective against this lesion and its phytid reactions, whether they harbor pathogenic fungi or not.

Foot baths (without iontophoresis) in solution of formaldehyde in 5 per cent or more concentration produce depression of sweat glands and have been used for many years in the treatment of dermatophytosis. However, in my experience the effect of formaldehyde on the sweat glands was more lasting when the solution was given by iontophoresis and fewer treatments were required. It was also my impression that formaldehyde was more effective in the treatment of dermatophytosis when administered by the iontophoretic current, although I have no proof of this point.

#### SUMMARY AND CONCLUSIONS

Eighty-five patients with epidermophytosis of all grades of severity were treated by the method of formaldehyde iontophoresis. The therapeutic response in patients whose disease

was of moderate severity was prompt and effective. The solution proved to be too caustic to be used in cases of severe infections in which the lesions exhibited denuded surfaces.

Fourteen patients with uncomplicated hyperhidrosis were treated with three daily treatments of solution of formaldehyde by iontophoresis with resulting complete remission of symptoms for approximately one month.

Thirty-five patients with dermatophytosis were treated with cupric sulfate solution by iontophoresis. The therapeutic response was good in cases in which the severity of the disease was moderate, but more treatments were required to effect a remission than with the use of formaldehyde. Cupric sulfate was well tolerated in cases of acute severe lesions exhibiting denuded surfaces. The results of treatment were good.

Iontophoresis was successful in the treatment of severe chronic phytid reactions when other methods of therapy had failed. Treatment should be applied to the phytid lesions as well as to the feet.

No serious toxic reactions were encountered in any of the treated patients.

My results indicate that the judicious use of formaldehyde and cupric sulfate iontophoresis produces a prompt clinical remission of dermatophytosis in approximately 75 per cent of cases. Data as to recurrences were not obtained in most cases because of inability to follow my patients for more than several weeks.

Major I. Arthur Mirsky, Medical Corps, Army of the United States, Lieutenant Colonel Donald M. Hudson, Dental Corps, Army of the United States, and Corporal William Erickson, Medical Department, Army of the United States, gave valuable advice and technical assistance.

# DIFFUSION OF WATER THROUGH DEAD PLANTAR, PALMAR AND TORSAL HUMAN SKIN AND THROUGH TOE NAILS

GEORGE E BURCH, M D

AND

TRAVIS WINSOR, M D

NEW ORLEANS

Since the observations of Erisman<sup>1</sup> in 1875 on the rate of diffusion of water through the skin of breasts and palms, studies of diffusion through dead human skin have been neglected and the rate of diffusion through toe nails has not been studied. In the study of insensible loss of water through the body and especially through the skin, it is important to know the relative ratio of water loss by diffusion through the skin of various portions of the body and nails.

## MATERIALS AND METHODS

The rate of diffusion was measured for dead skin collected from bodies within a few hours (one to twenty-four, usually three to four) after death. Only healthy-looking skin of well nourished nonedematous bodies was used. The skins were collected from the following areas of separate bodies: epigastrium of 9 different bodies, axillas of 5, plantar surfaces of 10, palms of 3, and nails of the big toe of 5 others. In most instances several samples of skin and nail were collected from the same body. The causes of death of subjects varied considerably including cerebral hemorrhage, accident (automobile), pneumonia, hepatitis, postpartal sepsis and chronic pulmonary tuberculosis. Occasional toe nails and plantar skin were collected from amputated feet.

The skins and nails were brought to the laboratory and mounted on a brass cylinder as shown in figure 1. The skin or nail was carefully prepared by the removal with surgical scissors of all fat, fibrous tissue and other subcutaneous and subungual tissue, leaving a relatively clean under surface. The skin or nail was then cut to cover the opening of the cylinder. It was then placed over the opening of the cylinder (c) which contained loose cotton and was filled with isotonic solution of sodium chloride. This solution filled the cylinders so that the fluid rested against the deep surface of the skin or nail. The cotton below provided means for the solution to keep in contact with the skin at all times, even with a decrease in the volume of fluid with evaporation. A brass ring (b) covered with a film of stopcock grease on the surface which came into contact with the skin was placed over the skin. Two pins soldered to the ring 180 degrees from each other were

slipped into loose-fitting holes properly placed in top of the cylinder (c). These pins prevented the brass ring and skin from twisting when the cap was screwed into place. The threaded portions were greased with stopcock grease. This tightly sealed a diaphragm of skin or of nail of 2 sq cm in area over the brass cylinder. This permitted loss of water only by diffusion through this known surface area of the skin or nail. Once the section of skin was in place the seal was intact, and the skin was not touched throughout subsequent weighings. The skin or nail mounted on the cylinder was placed in a room brought to desired temperature and relative humidity and allowed

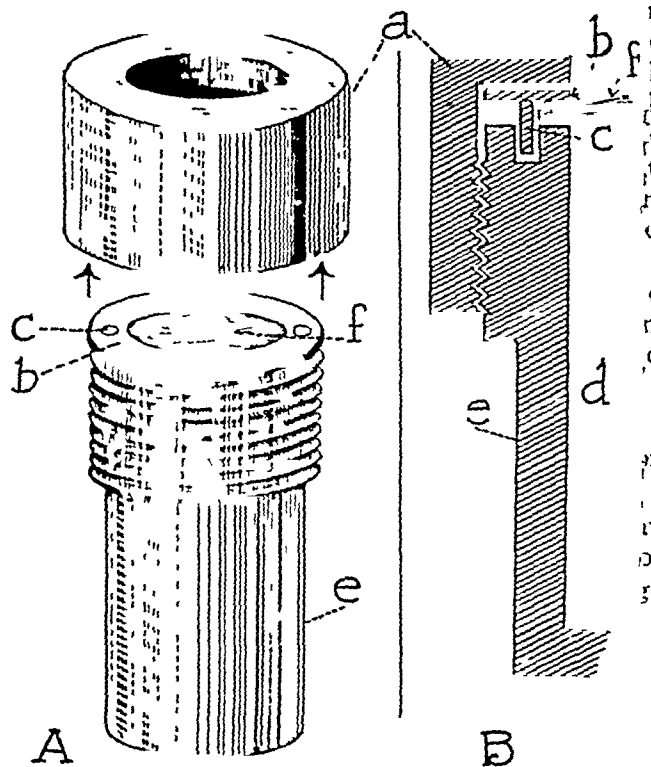


Fig 1—A diagram of the brass cylinders used in the measurement of the diffusion of water through skin. See text for details.

to dry for two to three hours. The metal cylinder with the tissue in place was weighed on an analytic balance to an accuracy of 0.1 mg. After a period of from a few minutes to twenty-four hours, usually four to five hours, the unit was weighed again. This was repeated several times over at least two successive days. Any loss of weight represented water lost by diffusion through skin or toe nail. The temperature and relative humidity of the room were varied to produce a cool comfortable room or a hot and uncomfortable one. The absolute values of these are shown in figure 2. Some of the cylinders with skin or nail mounted in place were put in fr

This is the seventh report from this Laboratory on Tropical Physiology.

From the Department of Medicine Tulane University Medical School and Charity Hospital.

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1 Erisman F. Zur Physiologie der Wasserverdunstung von der Haut. *Ztschr f Biol* 11:1 1875.

an ordinary electric fan at the various room temperatures and humidities in order to learn the influence of currents on the rates of diffusion

Some cylinders were filled respectively with whole blood, isotonic solution of sodium chloride and distilled water, with their surface exposed directly to atmosphere

In another study a piece of intact epigastric skin was placed over the cylinder and studied as previously described. Its corneous layer was then removed by the scraping and the rate of diffusion restudied

The area of epigastric skin was observed continuously sixty-one days under varying room conditions

diffusion of water as well as did an increase in temperature. A change in the humidity of the atmosphere did not produce as pronounced an influence on diffusion as did changes in temperature or air currents. An increase in the humidity of the air decreased the rate of diffusion

Diffusion of water occurred much more rapidly through epigastric skin with its corneum removed than through intact skin (fig 2). The rate was much more rapid from uncovered whole blood, isotonic solution of sodium chloride and

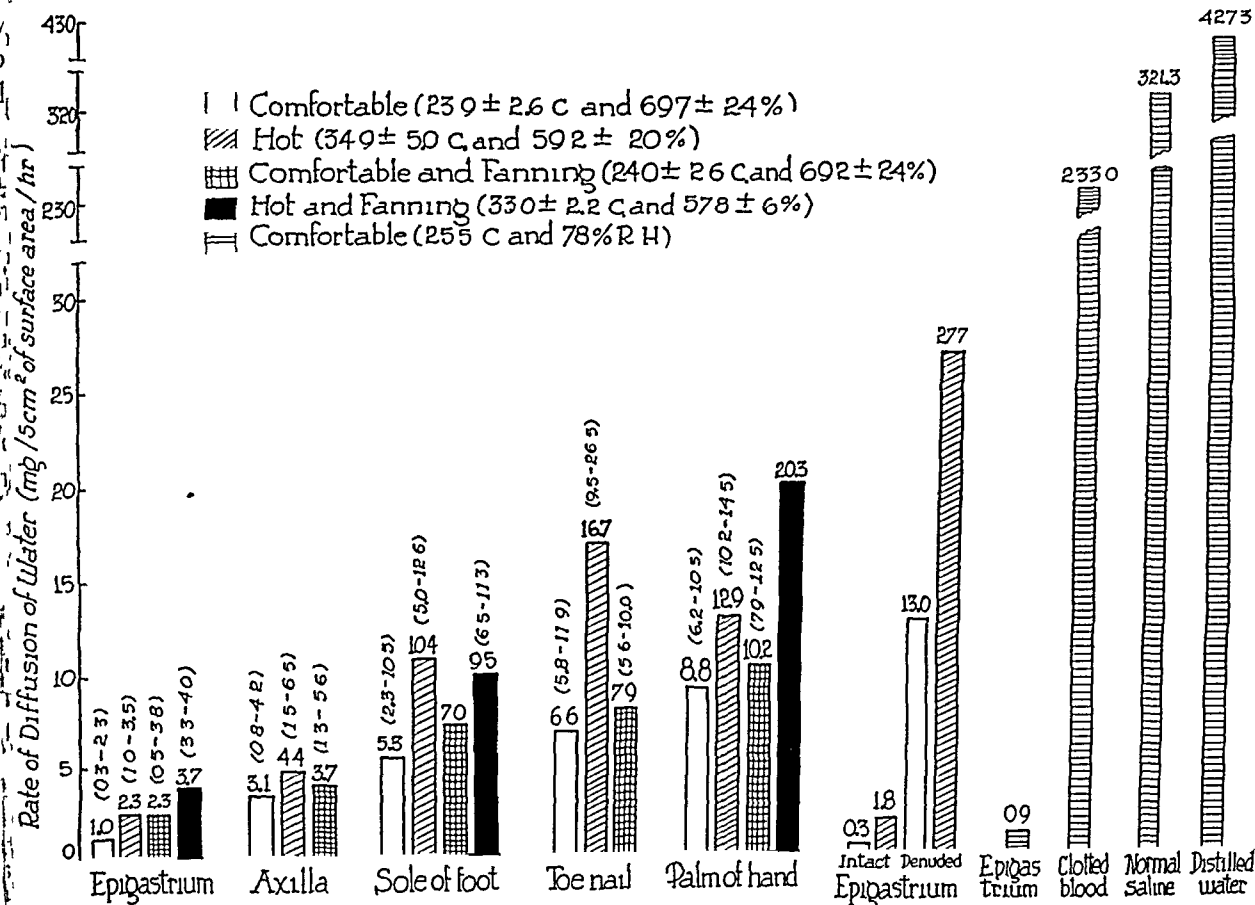


Fig 2—The rate of diffusion of water measured at various room conditions through skin from various portions of the body, including toe nails and intact epigastric skin immediately before and after denudation (removal of the corneum) and also from uncovered surfaces of fluids. The rate of diffusion of water through epigastrium and the uncovered surfaces of fluids shown to the left of the figure were measured simultaneously under similar room conditions

Many observations were made of each skin or nail at each room condition. Several hundred measurements were made in all, much too many to be presented in detail

## RESULTS

The results are summarized in figures 2 and 3. The absolute values are shown in the figures. The rate of diffusion of water through the epigastric skin was found to be much slower than that through any of the other skins or the toe nail. Diffusion of water took place most rapidly through the skin of the plantar and palmar surfaces. It occurred through the toe nail at a rate equal to that through the plantar and palmar skins. Fanning increased the rate of

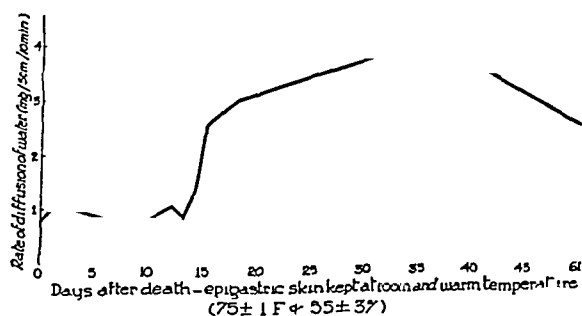


Fig 3—Variations in the rate of diffusion of water through a sample of skin from the epigastrium studied continuously for sixty-one days. The room conditions were temperatures, 24 ± 2 C, and relative humidity, 69.2 ± 2.0 per cent

distilled water (these fluids are listed in an ascending order of the rates of diffusion of water) than through epigastric skin (fig 2)

Figure 3 shows the influence of time on the inhibiting influence of skin to diffusion of water through it. The rate of diffusion changed little for the first two weeks, then it increased about three times, remaining at this level for the next six weeks. The rate of diffusion of water through this skin was still much slower than that through fresh plantar and palmar skin, toe nails or the aforementioned uncovered fluids even sixty-one days after death.

#### COMMENT

The observations indicate the great faculty possessed by human skin to inhibit diffusion of water. This is in keeping with observations in previous studies.<sup>2</sup> This property resides mainly in the corneum, as shown again in these studies. The cylinders containing whole blood, isotonic solution of sodium chloride and distilled water lost water at a rate greater than three hundred times that through epigastric skin.

The greater rate of water loss by diffusion through skin of the palms, soles and the toe nails is difficult to explain. The chemical and the histologic constitution of the entire skin and of the corneum, in particular of the palms and soles, are different from those of epigastric skin. How such differences might explain the striking differences in the rates of diffusion of water is unknown. The relative proportions of alpha and beta keratin in these tissues has not been determined, in fact, the physicochemical nature of skin is a much neglected aspect of biochemistry. The more rapid rate of diffusion of water

2 (a) Burch, G. E., and Winsor, T. Rate of Insensible Perspiration (Diffusion of Water) Locally Through Living and Through Dead Human Skin, *Arch Int Med* **74** 437 (Dec) 1944. (b) Winsor, T., and Burch, G. E. Differential Roles of Layers of Human Epigastric Skin on Diffusion Rate of Water, *ibid* **74** 428 (Dec) 1944.

through the skin of the palms and soles probably keeps these areas of skin slightly moist, thus facilitating the grasping of objects and walking. The difficulty one has in grasping objects securely when the palmar skin is dry is well known.

The epigastric skin studied for sixty-one days showed the prolonged efficiency of dead skin in the inhibition of diffusion of water. The fact that it changed little, even though pronounced digestive changes were noted in the underlying layers while the corneum merely wrinkled, is further proof that the corneum is the layer mainly responsible for the inhibition of the diffusion of water. The corneal layer is composed of dead cells even in intact living skin and therefore changes relatively little for several weeks after death. This layer has also been shown to be mainly responsible for the inhibition of diffusion of water in living intact skin.

The applications of these findings in health and in disease are obvious.

#### CONCLUSIONS

Our data support the following conclusions:

1 Diffusion of water occurs least rapidly through the skin of the epigastrium, most rapidly through the skin of the palms and soles and at a moderate rate through the skin of the axilla.

2 The rate of diffusion of water through the toe nail is essentially the same as that through the skin of the palms and soles.

3 Skin is an excellent barrier to the diffusion of water from the body, the corneum being the principle inhibiting layer.

4 Increases in temperature or air currents are especially effective in increasing diffusion, while changes in humidity of the air influence the rate of diffusion to a less extent.

5 Skin will retain its inhibiting influence on diffusion for many days (at least sixty-one days after death provided the corneum remains intact).

We were assisted in these studies by M. G. Morga



# THE ADRENAL GLANDS IN PEMPHIGUS VULGARIS

## REPORT OF A CASE

JOSEPH W GOLDZIEHER, M D

NEW YORK

In a previous paper<sup>1</sup> the literature on the histologic changes of the adrenal glands in pemphigus was reviewed, and the findings in 6 cases seen at New York City Hospital were presented. Progressive severe destructive changes with subsequent cirrhosis were found in all cases, the acuteness and extent of the lesions corresponding to the duration and severity of the disease. Since that time I have been able to study the adrenal glands in another case of pemphigus, and the findings were so unusual that I shall now present them.

tracts (10 to 15 cc a day) and vitamins given parenterally, the temperature dropped to normal, and the patient, who had appeared moribund, showed decided improvement. The temperature rose again slightly after penicillin was discontinued, but the lesions continued to heal. Cortical extract was gradually reduced and discontinued entirely after eight weeks. Thereafter the course was progressively downhill, and although large doses of penicillin were given, the temperature rose steadily, anorexia and vomiting appeared, and death occurred about twelve months after the onset of the disease.

*Autopsy*—Permission was granted for examination of the adrenals only. The right adrenal gland was in



Fig 1—Nodules of cortical cells of the left adrenal gland embedded in rather fibrous areolar tissue. Hematoxylin-fuchsin-Mallory stain  $\times 18$

## REPORT OF CASE

*History*—A 34 year old Jewish woman was admitted to the hospital with a five to six months' history of generalized bullous lesions which had extended to the oral mucosa, producing severe pain, nausea and dysphagia. Intensive therapy with vitamin D (100,000 units a day) did not help, and despite the addition of penicillin, the patient grew rapidly worse. Three days after institution of therapy with adrenal cortical ex-

From the Laboratory of Pathology, City Hospital, Welfare Island, Department of Hospitals, New York.  
1 Goldzieher, J. W. The Adrenal Gland in Pemphigus Vulgaris. Report of Six Autopsies and Review of the Literature. Arch. Dermat. & Syph. 52:369 (Nov-Dec) 1945.

its usual position, it was soft and about a third of the usual size. The cortex was less than a millimeter in thickness and of a brownish color with a delicate yellow peripheral zone. No gross hemorrhage was found. The left gland was absent, and in its place there was some rather fibrous perinephric fatty tissue in which a few yellowish nodules, up to 2 mm in diameter, were embedded.

*Microscopy*—The fat tissue surrounding the right adrenal gland was hyperemic. The capsule was irregularly thickened and sent strands of connective tissue down into the parenchyma. Considerable hematogenous pigment was present, and occasional small nests of cortical cells lay within the capsule itself. The parenchyma of the gland was collapsed, and there were numerous thick fibrous scars in the deeper layers.

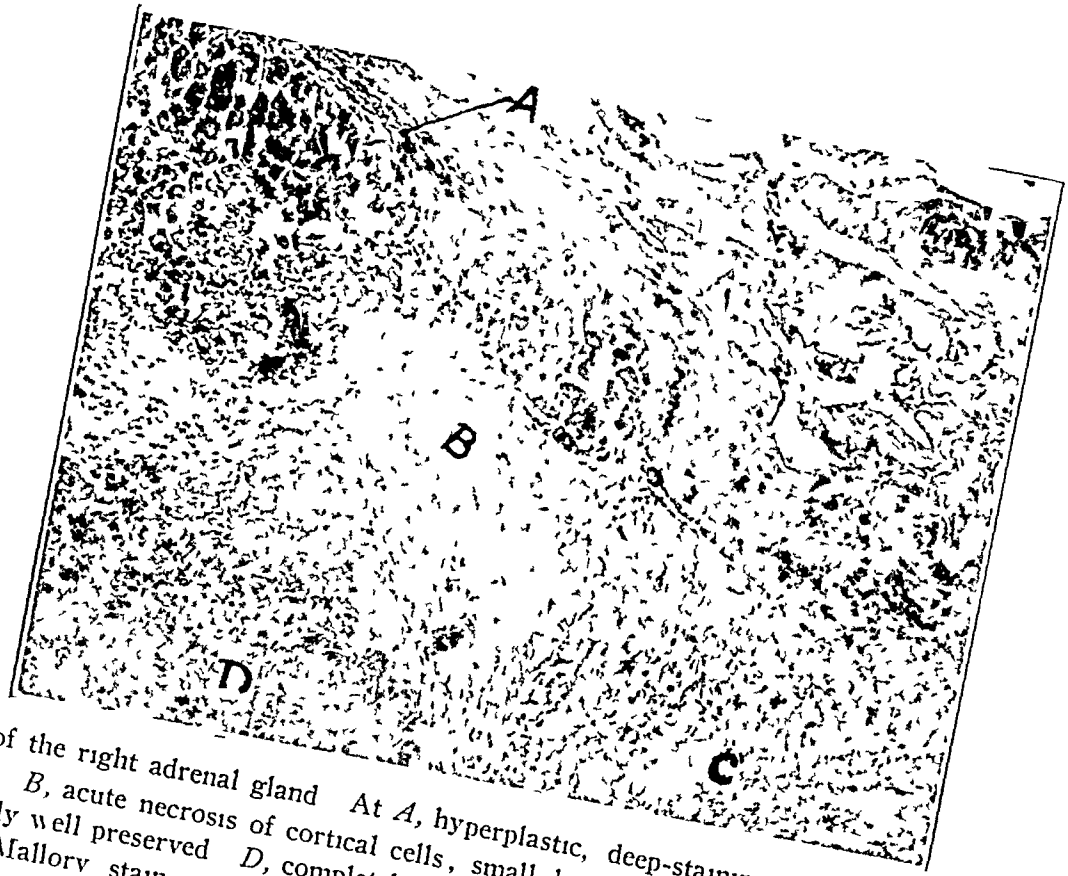


Fig 2—Section of the right adrenal gland At A, hyperplastic, deep-staining cortical cells with hemorrhage in the deepest layers B, acute necrosis of cortical cells, small hyperplastic nodule just above C, disorganized cortical cells still fairly well preserved D, completely necrotic tissue Note also the irregularly thickened capsule Hematoxylin-fuchsin-Mallory stain  $\times 50$

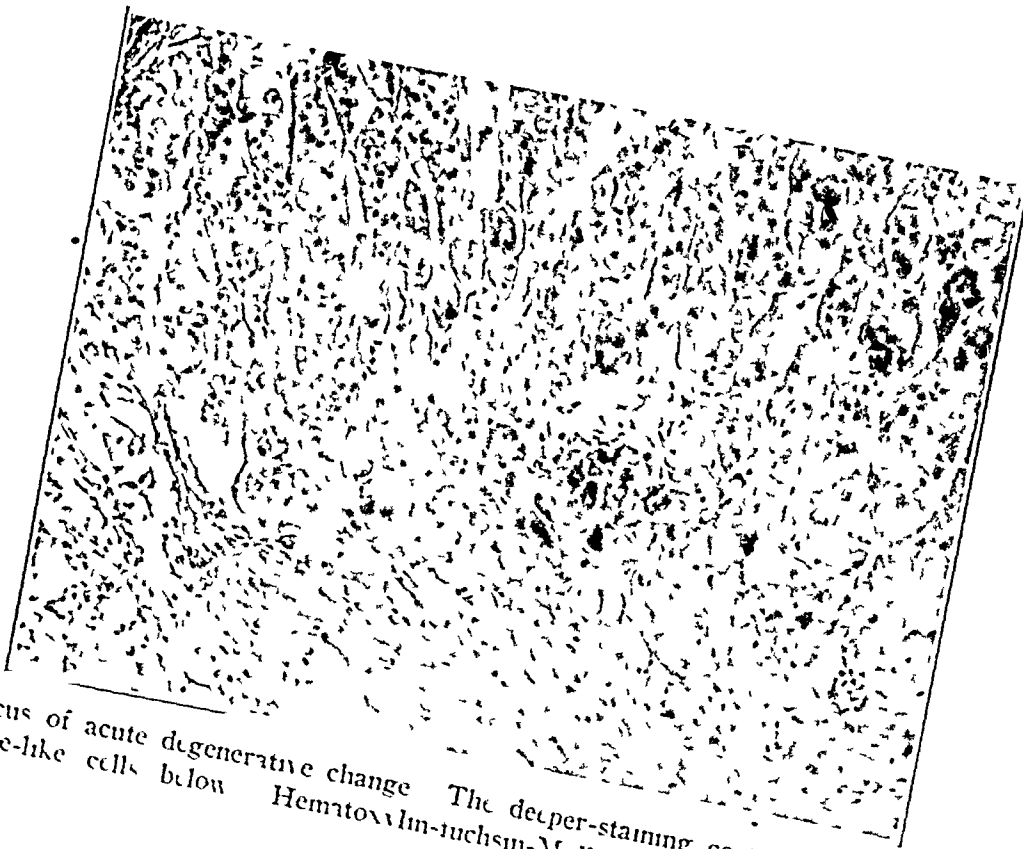


Fig 3—Small focus of acute degenerative change The deeper-staining cortical cells appear above and disorganized spongiocyte-like cells below Hematoxylin-fuchsin-Mallory stain  $\times 125$

neath the capsule there was occasionally a thin layer collapsed, pyknotic cells still faintly resembling spongiocytes. In many areas there was fresh hemorrhage, in others hematogenous pigment. Elsewhere there were small subcapsular nodules of hyperplastic cortical cells which, though deeply stained, showed acute degenerative changes. The major portion of the gland consisted of deeply staining necrotic material showing shadowy outlines of the architecture near the periphery but becoming completely homogeneous toward the center.



Fig 4—Organized thrombus in the lumen of a vein within the necrotic zone. Hematoxylin and eosin stain.

In this mass there were occasional clumps of bacteria, and in one place the walls of a vein were still discernible. Within the lumen of this vessel were the outlines of an organized thrombus (fig 4). No medulla could be seen in any of the sections.

The areolar tissue from the left side showed many dense scars containing a little blood pigment and occasional isolated nests of cortical cells. Near the fibrotic areas were more or less well encapsulated nodules of cortical tissue. Most of the cells within these nodules were fairly large, their cytoplasm stained intensely, mitoses were frequent. Rarely a few spongiocytes were seen, but for the most part the evenly stained cells showed acute degenerative changes in all stages. In some of these nodules there were fresh hemorrhages, in others, small fibrous scars. A large sympathetic ganglion nearby showed no changes.

#### COMMENT

The sequence of changes here appears quite clear. There was congenital malformation of the left adrenal gland, which was represented only by some scattered nodules of cortical tissue which were highly inadequate from the functional point of view. On the right side, the major portion of the gland had been destroyed by a thrombosis of not too recent date. The peripheral tissue showed both acute and chronic degenerative changes with fibrosis and some evidence of nodular regeneration. Judging from the histologic picture, there was really no functional cortex left, the medulla had been entirely destroyed.

#### SUMMARY

In a patient with pemphigus vulgaris, who during a period of therapy with adrenal cortical extracts showed good response but who died after discontinuation of treatment, there was found at autopsy a congenital malformation of the left adrenal gland and extensive destruction of the right gland. The pathologic process was similar to that described in detail in a previous publication.<sup>1</sup>

# Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

THE LOCAL CHEMICAL PROPHYLAXIS OF EXPERIMENTAL SYPHILIS WITH PHENYL ARSENOXIDES HARRY EAGLE, RALPH B HOGAN and RALPH FLEISCHMAN, *Am J Syph, Gonorr & Ven Dis* 28:661 (Nov) 1944

Nine trivalent arsenicals (phenyl arsenoxides) were studied with respect to their prophylactic activity in rabbit syphilis. Five-tenths cubic centimeter of solutions of the various arsenicals and propylene glycol were rubbed for four minutes on a superficial incision in the skin at varying intervals before and after its inoculation with a suspension of *Treponema pallidum* (Nichols strain) containing 10,000,000 organisms per cubic centimeter.

All the compounds were found to be effective and approximately in proportion to their direct treponemocidal activity. The concentration of the compounds necessary to protect half the animals treated four hours after inoculation varied from 0.06 to 0.15 per cent in the case of the more active compounds to 1.5 per cent in the case of the least active compound.

The effect of the p-CONH<sub>2</sub> phenyl arsin oxide, and presumably of the other arsenoxides tested, was due to a direct treponemocidal action on the organisms in the skin itself and not to a systemic effect.

The stability of the selected compounds, the intervals of time over which they remain effective, the low concentrations and the absence of local irritative effects at these concentrations, all offer promise that some of these compounds may be of value in the prophylaxis of the same disease in human beings. REUTER, Milwaukee

DERMATOLOGICAL PROBLEMS IN TROPICAL THEATERS Editorial, *Bull U S Army M Bull* 4 299 (Sept) 1945

This article briefly outlines the salient features of experience accumulated during this war and does not discuss the exotic tropical dermatoses. The following dermatologic diseases have been outstanding: (1) eczematoid dermatitis with secondary pyogenic infection, (2) the atypical lichen planus syndrome characterized by a combination of eczematous plaques and hypertrophic violaceous lichenoid lesions, (3) bullous impetigo, (4) ulcerative pyogenic lesions, (5) superficial fungous infections, (6) contact dermatitis due to the sap of various trees, (7) cutaneous diphtheria, (8) miliaria, (9) furunculosis, and (10) acne vulgaris, seborrheic dermatitis, psoriasis, atopic dermatitis, and all forms of localized eczema, which tend to become worse in hot humid climates.

The following general principles of dermatologic diagnosis and treatment were found to be important in the tropics:

1. Overtreatment with irritating and sensitizing drugs causes more disability than the primary diseases. In particular, tincture of iodine, Fraser's solution (salicylic acid, benzoic acid, tincture of iodine and spirits of camphor), sulfonamide ointments, strong salicylic acid preparations and ointment of benzoic and salicylic acid or any medication which causes even a questionable exacerbation should be discontinued immediately.

2. The pyogenic dermatoses are important causes of prolonged disability, especially if they are neglected and become well established. Sulfonamide ointments should not be used.

3. Patients with eczematoid lesions particularly of hands, feet and groin cannot be treated on an ambulatory basis.

4. Therapeutic agents such as sulfonamide compounds, arsenicals, quinacrine hydrochloride and quinine should be withheld or given with caution to patients with cutaneous diseases which might be caused by sensitization to drugs.

5. So far as possible, ulcerative lesions should be considered on an etiologic basis.

6. Heavy ointments and pastes, occlusive dressings and preparations containing more than 3 per cent salicylic acid are not well tolerated in the tropics.

7. The etiologic role of fungi should not be overemphasized, because it leads to failure to consider other etiologic factors, such as pyogens, contacts, psychosomatic factors and other endogenous drug and food allergens. STRAKOSCH, Denver

AN INTRADERMAL REACTION AS AN AID IN THE DIAGNOSIS OF GRANULOMA INGUINALE B. A. KORNBLITH, *New York State J Med* 44 2476, 1944

The test material is prepared in the following manner: A fair-sized piece of tissue is removed and triturated in a small amount of isotonic solution of sodium chloride in a sterile mortar. After proper dilution it is bottled and heated at 60 C for two hours on one day and 16 hours in the refrigerator over night. It is heated at 60 C for one hour on the following day. After being tested for sterility it is ready for an intradermal injection of 0.1 cc. The result is observed in forty-eight hours. If negative, there is no reaction; if positive, a tender nodule with an erythematous halo of variable size will appear.

RAPID PLAN FOR TREATMENT OF EARLY SYPHILIS FOR OFFICE PRACTICE A. B. CANNON, J. K. FISH and L. WEALER, *New York State J Med* 44 25, 1944

After a review of the subject of intensive treatment of early syphilis, two plans are described. The first, the twelve day treatment, consists of two daily intravenous injections of oxophenarsine hydrochloride (total of from 1.2 to 1.68 Gm, according to the patient's weight) and 100 mg of bismuth twice a week. The second, the daily or clinic plan, consists of daily (five days) syringe injections of arsphenamine or of oxophenarsine hydrochloride for twenty days. These plans are specially devised for use by the general practitioner in the treatment of primary and secondary syphilis in office practice. RONCHESF, Providence, R I

POWDERS AND CAPSULES HARPA L. KENDALL, *Purd Pharm* 22 39 (Dec) 1944

In the compounding of prescriptions for powder difficulties often occur because of the presence of sol-

stances which liquefy when triturated together or cause of the presence of a moisture-absorbing drug. Sometimes trouble is encountered as a result of the prescribed ingredients.

Some of the commonly used materials which liquefy in the presence of each other are menthol, camphor, eucalyptol, thymol, phenyl salicylate, chloral hydrate, resorcinol, chlorobutanol, pyrogallol, acetanilid, beta-naphthol, antipyrine, acetophenetidin, sulfonmethane, monomethylmethane, aminopyrine, salicylates, ethyl carbonate and urea. Such substances are generally referred to as "eutectics."

In the past, lactose and starch have been used exclusively for preventing liquefaction in powder mixtures. Sometimes heavy magnesium oxide, light magnesium oxide, magnesium carbonate and purified talc are used. It has been demonstrated from experimental work on various eutectic and deliquescent substances that light magnesium oxide and magnesium carbonate yielded the best results of any of the powders aforementioned. Heavy magnesium oxide and purified talc gave the next best results, while lactose and starch give the poorest. For substances which liquefy readily when triturated together, it is better to triturate them together first, add the liquid and then adsorb the liquid by the use of either bentonite or kaolin. Bentonite is a much better adsorbing agent than kaolin. Both are practically inert chemically.

RATTNER, Chicago

OBSERVATIONS ON SCABIES AT THE ST PANCRAS BATHING CENTER. M G GEFFEN, Brit M J 2 825 (Dec 23) 1944

During 1943 the author treated 1,136 school children with new cases of scabies, 201 children of preschool age and 442 adults by having benzyl benzoate painted on by a trained personnel at a clinic. Seventeen per cent of the school children returned to the clinic with recurrences. Among the adults and younger children 10 per cent returned with active scabies.

Investigation of the 52 recurrences in the latter group revealed that 22 occurred in families in which no contact had not been treated, 10 more patients knew that they had been in contact with scabies outside their homes while the 20 remaining could give no information revealing any source of reinfection.

Owing to a failure in the boiler system it was found impossible to give the usual preliminary bath to the school children attending for treatment. It was interesting to observe that there was no falling off in the cases during or soon after this period.

Scrubbing the skin to open burrows and lesions has been abandoned, the only apparent difference being that children with secondary sores no longer suffer as they do under this infliction. Children under 12 months of age were treated with "Marcussen's ointment." Experience has shown that recurrent scabies is a disease caused by dirt and that treatment at home frequently fails.

BISMUTH THERAPY IN JAUNDICE DURING ANTISYPHILITIC TREATMENT. J R FORBES, Brit M J 2 852 (Dec 30) 1944

The author attempted to determine whether the continuation of injections of bismuth preparations materially delayed recovery of hepatic function in cases of jaundice due to therapy.

One group of patients received intramuscular injections of bismuth the other did not. Arsenicals were not given to either group while jaundiced. In all other respects the groups were comparable.

The Quick hippuric acid excretion test was employed as a test of recovery of hepatic function. The results strongly suggest that bismuth does not retard recovery of hepatic function and support the view that bismuth therapy should be continued in the presence of jaundice of this nature.

DERMATITIS FROM ARMY SPECTACLES. W O G TAYLOR AND A G FERGUSON, Brit M J 2 40 (July 14) 1945

The authors report on 6 persons having a dermatitis after wearing nickel-framed spectacles. Investigation showed that nickel-silver alloys were the cause of a specific hypersensitivity. The most satisfactory solution of the problem was to change to gold or shell frames or to attach a protecting wafer or "washer" to the frames.

OTITIS EXTERNA. J F BIRRELL, Brit M J 2 80 (July 21) 1945

On the basis of nearly 1,000 cases of otitis externa observed in the army, the author makes a number of recommendations. Meatal congestion may be caused by (1) irritants which enter the meatus from the middle ear, (2) the natural secretions of the meatus, (3) irritants entering the canal from the outside, (4) general conditions predisposing to cutaneous infections or (5) local or general allergy. In this series *Pseudomonas pyocyanea* was the predominant organism in nearly every case in which bacteriologic studies were made. The prognosis in any attack of otitis externa was good. In 60 to 70 per cent of the cases there was healing within a week. However, relapses were common, and frequent recurrences or lack of early treatment led to chronicity, which, once established, made the disease almost impossible to be cured. Treatment is based on two procedures: first, the thorough cleansing from the meatus of all particles of discharge, and, second, the application of lotions to the inflamed meatal walls. Drugs should be applied on wicks of ribbon gauze or painted on by means of wool-tipped wire probes. Cotton should not be used. In the acute edematous cases the author prefers ichthammol (10 per cent) in hypertonic solution of sodium chloride. He recommends ichthammol (10 per cent) in glycerin to be used after forty-eight hours of treatment until there is no further exudation. At this point, silver nitrate (1 per cent) or an alcoholic solution (1 per cent) of gentian violet medicinal should be used to harden the meatal skin.

Associated dermatitis of the auricle is best treated with ammoniated mercury (1 per cent) in paste of zinc oxide applied on spreads and moulded to the pinna. Penicillin is of little value, since in most cases the disease is caused by a mixed infection.

The patient is instructed not to scratch the ear, however itchy, and not to let water enter the meatus during washing. Sea bathing is forbidden.

SHAW, Chattanooga, Tenn

A COMPARATIVE STUDY OF GAEHTGENS' PALLIDA REACTION WITH WASSERMANN AND KAHN REACTIONS. T CHING-CHIEN, Acta dermat-Venereol 21 578 (July) 1940

A comparative study was made on the sensitivity and specificity of the Gaetgens pallida complement fixation reaction with use of an antigen made of an emulsion of dead *Treponema pallidum* in 0.3 per cent solution of phenol in isotonic solution of sodium chloride, in

relation to the standard Kahn and Wassermann reactions. The author recorded results in 202 cases of syphilis and 413 cases of miscellaneous diseases other than of syphilitic origin. In the 202 cases of syphilis the Gächtgens reaction was positive in 92.4 per cent while the Wassermann reaction was positive in 74.7 per cent and the Kahn reaction in 94 per cent. The Gächtgens test detected positive reactions in 6 serums which reacted negatively to Kahn and Wassermann tests, while the Kahn test picked up positive reactions in 7 serums which reacted negatively to Gächtgens and Wassermann tests. In the nonsyphilitic serums three false positive reactions were elicited by the Gächtgens test, thirteen by the Kahn and none by the Wassermann test. The included table demonstrated that the Gächtgens pallida reaction is more sensitive and less specific than the Wassermann reaction but less sensitive and more specific than the Kahn reaction.

SUPERFICIAL BASAL CELL EPITHELIOMA. A. MADSEN,  
Acta dermat-venereol., 1941, supp. 7

By means of horizontal serial sections (in 10 cases of superficial basal cell epitheliomas) involving sixteen separate sections of tissue, the author presents a new theory of the origin of these lesions.

In preparing these sections of tissue the excised portion of skin was stretched across a plane piece of wood, fixed in this position in 40 per cent solution of formaldehyde and then embedded in either paraffin or celloidin. Serial sections of the tissue were then made horizontal to the surface of the skin. The paraffin sections were cut 8 to 10 microns thick, while the celloidin sections varied from 14 to 20 microns. All sections were stained with hematoxylin and eosin. These were then studied by plastic reconstructions and projection drawings.

All the developed superficial basal cell epitheliomas showed the same structure. There is a peripheral band of neoplastic tissue which is either continuous or broken by comparatively short interstices. Within the confines of this peripheral ring are clusters of tumor parenchyma which are either isolated or continuous with each other or with the concave border of the peripheral ring. Practically all portions of the tumor parenchyma are in intimate contact with the epidermis, which within the border of the epithelioma lacks the normal interpapillary processes or ridges. The depth of the tumor does not exceed 0.2 to 0.3 mm and the width 1 to 2 mm. The cells in the inner curve of the peripheral ring show signs of degeneration and young connective tissue is seen growing inward between the cancer cells. Young connective tissue with an infiltrate of lymphocytes and plasma cells form the stroma of the tumor, with a collection of polymorphonuclear leukocytes immediately beneath the ulcerations. Considerably increased melanin deposits were found in the neoplastic cells, stroma and normal basal cells immediately surrounding the edge of the tumor while the thinned epidermis covering the tumor showed little or no pigment.

Madsen contests the previously accepted theory based on histologic observations and models of Petersen that the tumors are of multicentric origin and originate in the hair follicles or interpapillary processes in multiple foci. He is rather of the opinion that the tumors are of unicentric origin originating in a single epithelial cell located in some point in the interpapillary process of the epidermis. As the tumor grows the interpapillary processes are destroyed. In the center of the growth cells die in masses and their places are then occupied by young connective tissue cells. This process leaves isolated islands and irregular trabeculae of epithelial tissue, some of which may be connected with hair follicles, surrounded by a more or less continuous peripheral ring of neoplastic parenchyma. It is easy to understand how this picture could be interpreted as being of multicentric origin in the ordinary type of histologic sections.

ROBINSON, Washington D. C.

## News and Comment

### COURSE IN HISTOPATHOLOGY OF THE SKIN

The following course for former medical officers whose training in Dermatology was interrupted by military service will be available at the Columbia University College of Physicians and Surgeons, New York. HISTOPATHOLOGY OF THE SKIN. By Dr. Gerald Machacek.

The course will consist of three hours of lectures and six hours of laboratory work per week and will be given on Monday, Thursday and Friday from 2 to 4 p. m., from April 1 to May 31, 1946.

Enrollment will be limited to ten students.

The fee is \$100.

Further information may be obtained from the Director, Columbia University College of Physicians and Surgeons, New York 32, N. Y.

### GENERAL NEWS

**American Board of Dermatology and Syphilology, Change in Date of Examination**—The oral examination for both A and B candidates will be held in San Francisco on June 28 and 29. The written examination for group B will be held on April 22. The closing date for applications is March 1.

It is probable that a second examination will be held in December about the time and at the place of the next meeting of the American Academy of Dermatology and Syphilology.

### DEATHS

Dr. Alfred Potter died at his home in Brooklyn Dec. 27, 1945.

Dr. Harry Bailey died suddenly at his home in Hartford Conn., on Jan. 19, 1946.

## Society Transactions

### HAWAII DERMATOLOGICAL SOCIETY

JAMES T. WAYSON, M.D., *President*†

HARRY L. ARNOLD JR., M.D., *Secretary*

June 3, 1944

#### Lupus Erythematosus Superimposed on a Nevus

Presented by DR. HAROLD M. JOHNSON

J. D., a 30 year old Filipino, was first seen on June 1, 1944, with a bright red elevated verrucous scaly lesion located in a curved scimitar-like smooth brown lesion, which has been present since birth. The birthmark suddenly became rough and scaly about one year ago. The lesion is aggravated by exposure to sunlight, evidenced by burning, itching and swelling. The lesion is sickle shaped and about  $\frac{1}{2}$  inch (1.3 cm) in width and extends from the right supraorbital area forward into the scalp. There are scaling and follicular plugging. The blood was normal, except for 5 per cent eosinophils. There was no leukopenia.

**Biopsy Report** (Dr. I. L. Tilden).—The sections are characterized by parakeratosis and sharply outlined patches of cellular infiltrate in the corium. The epidermis in certain fields is somewhat atrophic, and the hair follicles are moderately dilated. The infiltrate is polymorphous in character, with lymphocytes predominating. The histologic features are somewhat suggestive of lupus erythematosus, although the parakeratosis is against this diagnosis.

#### DISCUSSION

CAPT. HERBERT LAWRENCE, M.C., A.U.S. I think that this disease is a verrucous nevus because of my previous experience with a similar case and partly because of the histologic structure. I feel that it is not lupus erythematosus.

LIEUT. HARRY KATZ, M.C.-V(S), U.S.N.R. I think that the lesions on the right auricle strongly support a diagnosis of lupus erythematosus. I suggest a biopsy of one of these.

DR. HAROLD M. JOHNSON. The sudden onset of erythema and scaling and the dilatation and plugging of the follicles lead me to think that the disease is lupus erythematosus. The lesion is also aggravated by exposure to the sun.

DR. HARRY L. ARNOLD JR. What did the original nevus look like?

DR. HAROLD M. JOHNSON. The patient described it as a typical linear nevus, smooth and brown, prior to its change.

DR. HARRY L. ARNOLD JR. I agree with the diagnosis presented.

DR. JAMES T. WAYSON. I think that the disease is lupus erythematosus.

† Dr. Wayson died Jan. 17, 1945.

#### Pemphigus Vulgaris Presented by DR. HARRY L. ARNOLD JR.

Y. Y., a 52 year old Japanese man, was first seen on April 3, 1944. He had had sores on the gums and in the mouth for a year, and during the past month he had begun to have cutaneous lesions as well, first on the scalp and later all over the body. These were associated with considerable itching and burning. He presented a nearly universal eruption, consisting of flaccid superficial blebs 2 to 30 mm in diameter, rising out of uninfamed skin and usually rupturing readily and becoming covered with a foul-smelling crust. Nikolsky's sign, slipping at the dermoepidermal junction, could not be demonstrated but subsequently could be elicited.

The sedimentation rate was 26 per cent at one hour (normal 0.5 to 4 per cent), the Weltmann coagulation band was 7, and fell to 4 a week later, where it remained for some four weeks. Examination of the blood showed mild secondary anemia and 2 per cent eosinophils. Kolmer Wassermann and Eagle reactions of the blood were negative.

Histologic section of a bleb showed it to occupy the epidermis itself, with a thin layer of distorted hydropic prickle cells and basal cells beneath it. The vesicle contained a number of similar hydropic cells, a number of eosinophils and, in addition, two coherent masses of sebaceous gland material. The latter appeared to have been discharged into the vesicle in a most remarkable manner, at a point where the vesicle itself extended from its situation in the epidermis down the wall of a hair follicle right to the sebaceous gland orifice.

The patient was hospitalized and given sulfadiazine, plus hypodermic injections of solution of sodium arsenate. After five days of treatment with sulfadiazine he was much worse, and albuminuria and hematuria had developed, so use of the drug was stopped. On April 14, 1944, treatment with acetarsone was begun in a dosage of 0.1 Gm, three times a day, at this point the patient was much worse than at any previous time. The drug was given three days out of every five, and on the twelfth day the dose was increased to 0.6 Gm daily. On the thirteenth day the patient was perceptibly better, and by the fifteenth day of acetarsone therapy he was definitely improving. On the seventeenth day (May 1) the dose was increased to 0.75 Gm, taken before breakfast daily for three days out of five, and by May 5 he was so much better that his recovery was anticipated and he was given a series of blood transfusions to combat his secondary anemia. The Weltmann band had returned to 8, and it subsequently remained at that level, suggesting fibrosis, healing and cessation of exudation. He has had about two thirds of Oppenheim's recommended total dose.

NOTE.—The patient began to relapse about July 1 and died on July 15. Autopsy showed only moderate bronchopneumonia.

#### Pemphigus Vulgaris Presented by DR. HARRY L. ARNOLD JR.

A. C. A., an 80 year old white business executive, retired, was first seen on Oct. 13, 1943, because of what had been thought to be a severe fusospirochetal



stomatitis of about four months' duration. He had complained at irregular intervals of irritation of the pharynx, and of hoarseness on occasion, for at least three years. When he was seen he presented two or three ill defined erosions on the palate and near them an intact bulla, roughly 1 by 2 cm and nearly 0.5 cm high, without redness. A multiple puncture vaccination against smallpox was performed, and primary vaccinia resulted, but the lesions continued to appear at the usual rate of one every week or so.

At irregular intervals, a transitory bleb would develop on an arm or hand. Vesicle fluid from one of these showed 33 per cent neutrophils and 12 per cent eosinophilic polymorphonuclears, the blood at the same time showed only 6 per cent eosinophils. The sedimentation rate was subnormal (125 per cent), and the Weltmann coagulation band was 8 (right shift). Since Nov 24, 1943, the patient has been receiving injections of sodium arsenate, 1 cc of a 2 per cent solution by hypodermic injection twice a week. The lesions in the mouth slowly became smaller, more transitory and less frequent on this regimen, but occasional isolated cutaneous lesions continued to appear. In February 1944, the dosage was increased to 1.5 cc twice a week, and in April 1944, it was decreased by half, to 1.5 cc once a week.

On May 10, 1944, a bleb on the hand was partially excised for histologic study. It showed a vesicle which occupied the lower half of the epidermis, roofed by thin epidermis and floored by only a few scattered hydropic epidermal cells. The corium immediately beneath showed rather abundant polymorphonuclear and lymphocytic infiltration with numerous eosinophils.

#### DISCUSSION OF THE TWO PRECEDING CASES

DR HARRY L. ARNOLD JR. I am curious to know whether any one here has seen enough cases of pemphigus in remission to have an opinion regarding the probable length of the remission.

LIEUT. HARRY KATZ, MC-V(S), USNR. I have seen cases in the New York City Hospital which lasted for as long as seven years, but I do not recall that there was anything consistent about the duration of remissions.

DR HARRY L. ARNOLD JR. I presented the first case partly because it is an interesting example of an apparent therapeutic response to acetarsone and partly because pemphigus appears to be remarkably rare in Hawaii. Dr. Wayson tells me that in fifty years of practice here he has seen only 2 cases of pemphigus vulgaris, 1 of the patients was a white woman and 1 a Hawaiian woman. Both died.

MAJOR GERARD DE ORFO, MC, AUS. In regard to the second case, I think that the history of repeated attacks of relatively painless bullae in an aged person is consistent with the diagnosis of pemphigus. I should accept that diagnosis, particularly in view of the typical histologic picture.

DR HARRY L. ARNOLD JR. Is acetarsone too dangerous a drug to be used in a case of this sort?

MAJOR GERARD DE ORFO, MC, AUS. I think so. I would not use it for a man doing as well as this one is. In regard to the first case, that of the Japanese man, I suspect that he is going to have a remission which may last for weeks or months. Whether to continue the acetarsone or not is a question. I suggest saving it for his next relapse.

MAJOR SOLOMON GREENBERG, MC, AUS. It has been my impression that oral lesions in pemphigus indicate a bad prognosis. The second case therefore, is of particular interest because in spite of oral lesions

the patient is having only a mild form of the disease. In those cases which I have seen which began with lesions in the mouth, and I recall 2 at the moment, 2 patients had a severe spread of the eruption on the body some weeks afterward and died several months after the onset of the oral lesions.

#### Pityriasis Rubra Pilaris Presented by DR. HARRY L. ARNOLD JR.

J. M., a 10 year old Caucasian-Japanese girl, was first seen on May 26, 1944, because of a four month eruption confined to the upper part of the trunk. The eruption consisted of variously sized, sharply outlined groups from 1 to 15 cm in diameter, of closely set, skin-colored to pink, flat-topped, shiny papules about 1 mm in diameter. Many of them appeared to be follicular, but the follicular orifices were inconspicuous. The face and mucous membranes and the palms and soles were perfectly normal, as were the dorsa of the pharynges and the hands.

Biopsy showed three papules, two of them obviously follicular, there were moderate hyperkeratosis and patchy hyperkeratosis, the latter being conspicuous in the vicinity of the hair follicles. The corium showed a nondescript focal cellular infiltrate.

#### DISCUSSION

DR. HARRY L. ARNOLD JR. Dr. Irvin L. Tild made the diagnosis of pityriasis rubra pilaris independently from the histologic section.

DR. HAROLD M. JOHNSON. When I first saw this patient, I wondered whether she might have phrynodema on the basis of vitamin A deficiency. I think that the basilar degeneration in the section rules out this diagnosis and suggests that the disease is pityriasis rubra pilaris.

DR. HARRY L. ARNOLD JR. My impression is that phrynodema does not occur in such regular and sharply outlined patches, it is more diffuse and tends to be most pronounced on the backs of the arms and on the shoulders and thighs—areas which are virtually spared in this patient.

CAPT. L. H. ROSENTHAL, MC, AUS. I am inclined to regard this as lichen scrofulosus or a group trichophytid. Was a Mantoux test performed on this youngster?

DR. HARRY L. ARNOLD JR. No. I think that the diagnosis of lichen scrofulosus is a good suggestion, however, and perhaps the biopsy does not exclude it.

#### Amyloidosis of the Skin Presented by DR. HARRY L. ARNOLD JR.

P. G., a 42 year old white war worker, was seen on May 26, 1944, because of a severe inflammatory lymphadenitis of the left femoral region, which responded without suppuration to roentgen ray therapy and sulfathiazole taken by mouth. This appeared to be secondary to excoriations in a dermatosis which covered almost the entire left shin. This dermatosis had begun about four years before on the left shin and had later involved the right one as well but had subsequently faded from the latter side, leaving only faint "ghosts" of the former lesions. On the still involved side it was seen to consist of closely set brownish lenticular papules 2 to 4 mm in diameter, with moderate hyperkeratosis and a number of linear excoriations.

Histologic sections showed four closely set discrete papular lesions, each one presenting slightly more hyperkeratosis than in the intervening skin and each of



representing slight acanthosis as well. This was made more conspicuous by lateral compression of all the rete pegs by pink-staining amorphous material occupying the dermal papilla. This material suggested the diagnosis of amyloid to Dr Irvin L Tilden, and it was found to stain in a characteristic manner with congo red. Subcutaneous injection of congo red, 0.5 cc of a 1 per cent solution, was done into the involved area and into the normal skin above it and into the skin of the own leg as an additional control. The dye has not faded from the latter sites, hence the results of this test cannot yet be evaluated. However, even at forty-six hours the rose color is definitely deeper in papular lesions than in the furrows between them.

#### DISCUSSION

DR HARRY L. ARNOLD JR. Is spontaneous involution of lesions rare in this disease?

MAJOR GERARD DE OREO, MC, AUS. In 1939 I had a case just like this one (ARCH DERMAT & SYPH 605 [March] 1940) in which some of the lesions subsequently spontaneously disappeared. As a rule in these cases no generalized amyloidosis is present, and it was true of the case in 1939. Dr H. J. Parkhurst suggested that the eruption in that patient corresponded to that of lichen planus ocreiformis.

**Case for Diagnosis (Psoriasis, Parapsoriasis en Plaques [Brocq]?)** Presented by DR HARRY L. ARNOLD JR.

G. I., a 22 year old Chinese woman, was first seen in March 1944, because of a moderately pruritic papulopustular eruption on the elbows, neck and back, with a group of 3 oval nickel-sized soft, red, irritated plaques on the right side of the neck. The latter had appeared recently and their appearance, like their subsequent involution with residual hyperpigmentation, strongly suggested a fixed drug eruption though no corroborative history could be obtained. The other lesions were sharply outlined, oval, slightly raised, brownish, dry, scaly plaques, with scanty scale and no redness; the lesions on the elbow showed some tendency to confluence. The knees, scalp, face, mucosae, palms and soles were spared.

Histologic examination of a lesion on the buttock showed acanthosis, with fairly uniform length of the elongated rete pegs but highly variable width; the dermal papillae were unaltered, except for length, and none of them reached anywhere near the horny layer. The granular layer was interrupted in several places, with overlying patches of parakeratosis. The scale was not abundant and not at all lamellar. There was no leukocytic migration or microabscess formation in the epidermis. The corium showed rather abundant cellular infiltrate, with numerous eosinophils and plasma cells. Much of this was perivascular.

#### DISCUSSION

MAJOR SOLOMON GREENBERG, MC, AUS. What experience have the members had in regard to itching in patients with parapsoriasis? In last year's Year Book there were reports of cases which mentioned methods of relieving itching in patients with parapsoriasis. Pruritus is generally considered minimal in this disease. A patient of mine with what is probably the "en plaques" variety complains of considerable itching. In the 1942 Year Book there is an article mentioning the relief of pruritus in parapsoriasis in the course of treatment.

DR HARRY L. ARNOLD JR. My feeling is that itching in patients with parapsoriasis is rare. I think that perhaps some cases of so-called parapsoriasis en plaques with itching are really examples of premycotic mycosis fungoides.

CAPT L. H. ROSENTHAL, MC, AUS. I think that pruritus is purely relative, more easily elicited in some patients than in others. It is true that there have been cases of parapsoriasis described in which pruritus was a prominent feature.

DR HAROLD M. JOHNSON. My diagnosis in this case is disseminated neurodermatitis.

CAPT HERBERT LAWRENCE, MC, AUS. I agree with Dr Johnson's diagnosis. I think that the woman's personality and history suggest neurodermatitis.

**Tuberculoid Leprosy** Presented by DR HARRY L. ARNOLD JR.

W. C. R., a 47 year old white housewife, was first seen in June 1941, because she had concluded from a study of the "Encyclopaedia Britannica" that she must have leprosy. The lesions consisted of a raised reddened plaque and two raised reddened annules, all about the size of a dime, situated close together just above and anterior to the external epicondyle of the right elbow. She had first noticed these about ten years before, and they had changed little during this period. About six months before coming to the office she had noticed numbness in the region of the right elbow. Tissue juice obtained from the lesions by the scraped incision method had shown no acid-fast bacilli.

Sensory examination showed tactile anesthesia in an oval zone enclosing these three lesions and in a triangular area just below the olecranon; there was also thermal anesthesia in a much larger zone enclosing the latter area and extending down the ulnar edge of the forearm, as well as in a few small areas on the right hand. The ulnar nerves seemed quite normal to palpation, no other superficial nerve trunks could be felt, and there were no lesions or areas of anesthesia elsewhere. Tissue juice was obtained again and showed no acid-fast organisms.

Biopsy revealed characteristic epithelioid tubercles, with a sprinkling of lymphocytes, acid-fast stains of the sections failed to reveal any acid-fast bacilli.

A year later the patient was seen again, with some pain in the right arm, which was thought to be a specific (leprosy) neuritis and which responded promptly to intravenous injections of thiamine hydrochloride.

#### DISCUSSION

MAJOR GERARD DE OREO, MC, AUS. Were there trophic changes in the skin just below the elbow?

DR HARRY L. ARNOLD JR. I think so. That area is anesthetic and presumably anhidrotic as well, and it is a little thin and shiny.

MAJOR GERARD DE OREO, MC, AUS. Is that because of involvement of the nerve trunk?

MAJOR EDWIN K. CHUNG-HOON, MC, AUS. I think that the disease is rather a multiple involvement of the finer branches of nerves in that area. I think that the patient's most serious trouble is neurosis. Dr Arnold sent her to me about three years ago, and I found at that time essentially the same condition that she presented today. I felt then, as I feel now, that the clinical picture was strongly suggestive of leprosy but that her most serious problem was her fear of being a "leper." I thought that it would do more good to reassure her than to commit her since, in the light of

present day knowledge of the disease, her condition is considered to be in the noncommunicable form. So I merely told her not to worry about it, and made certain that she would be kept under observation.

DR IRVIN L. TILDEN (by invitation) Biopsy at that time showed histologic changes typical of tuberculoid leprosy.

DR HARRY L. ARNOLD JR. There appears to have been no progression whatever of the cutaneous tuberculoid lesions, although the nerve lesions have progressed somewhat, as indicated by a considerable enlargement of the anesthetic area on the forearm. I am still inclined to believe that removing these three little "macules" from her arm and from her sight would do the patient a great deal of good.

MAJOR GERARD DE ORO, MC, AUS. Would freezing with solid carbon dioxide help lesions like these?

DR JAMES T. WAYSON. I think that it would help them.

CAPT L. H. ROSENTHAL, MC, AUS. I think that for a patient with this temperament the less one does to the skin the safer one is.

#### Tuberculoid Leprosy Presented by DR HAROLD M. JOHNSON

W. T., a 14 year old girl, was first seen on May 15, 1944, with a history that in December 1943, she first noticed an irritation which followed a burn on the dorsum of the foot. The lesion healed fairly well but remained extremely tender to touch. There has been little change during the last six months. She has complained of lancinating pains along the lateral side of her foot and leg. The patient is a member of a modern and prosperous Chinese family who came to Hawaii from Canton, China, in 1940.

There is a dark red, slightly elevated, moderately infiltrated, irregularly outlined cutaneous lesion about  $1\frac{1}{2}$  by 3 inches (3.8 by 7.6 cm) in size on the lateral half of the dorsum of the left foot. A large infiltrated cutaneous nerve is visible and palpable over the dorsum of the left foot, extending from the lateral aspect of the foot just below the external malleolus across the foot and then lost in the skin about the midline. The nerve is about the size of an ordinary lead pencil, fusiform and moderately tender. The involved area of this foot is anesthetic to thermal and tactile stimulation. There is also a history of acute neuritis of the left lower extremity, apparently involving the superficial peroneal nerve.

*Biopsy Report* (May 29 1944, DR I. L. TILDEN) — Frozen sections were made and these show interesting changes. The fundamental change is focal accumulation of epithelioid cells and lymphocytes. Most of these are rather superficial, and some are confluent. They are concentrated especially about cutaneous appendages and nerve trunks. In some of them involution has taken place with fibrous tissue replacement. The epidermis shows moderate hyperkeratosis and accentuation of the granular layer. There is no acanthosis. The histologic features are highly suggestive of tuberculoid leprosy, however, I should like to prepare paraffin sections and stain them for acid-fast organisms before making an absolute diagnosis.

#### DISCUSSION

MAJOR EDWIN K. CHUNG-HOON, MC, AUS. This is about as early a lesion of leprosy as one is ever likely to see. I think that Dr. Johnson is to be congratulated on making the diagnosis on the basis of such early evidence. The chief signs and symptoms in

this case are anesthesia, a cutaneous lesion and enlargement of a cutaneous nerve. Even though acid-fast organisms were not found in the tissue juices of the cutaneous lesion, a diagnosis of leprosy can still be made from the evidence at hand.

DR HAROLD M. JOHNSON. I have told the patient's father the diagnosis and advised him that the outlook is good. I advised him to keep the child at home and to bring her in for examinations regularly. I think that it would be a good idea to test her with lepromin for its prognostic significance. I understand that Dr. Tilden has prepared a supply of this material.

DR HARRY L. ARNOLD JR. If I had this lesion I should certainly feel better if I knew that I had a strong reaction to lepromin.

DR JAMES T. WAYSON. I do not think that you would. I advise that this test not be performed at all. Even after one has made it, one still does not know where one stands. I should simply keep this patient under observation, seeing her about once a month.

DR HARRY L. ARNOLD JR. What about allowing her to go to school?

DR JAMES T. WAYSON. Certainly I would let her go to school. I think that in a case like this the patient is entitled to the benefit of the doubt. This girl may have leprosy, but there is no absolute proof of it. Whether she has it or not, she is certainly not a source of danger to other people. If one lets a palpable nerve lead one to a diagnosis of leprosy, one will be swamped with doubtful cases. Take the great auricular nerve, for example. In routine school examinations palpable great auricular nerves are found in many children, and they disappear after a while. It cannot be said that in all cases palpable auricular nerves or any other palpable nerves are due to leprosy.

MAJOR EDWIN K. CHUNG-HOON, MC, AUS. Because of the neuritis it might be a good idea to give this girl thiamine hydrochloride intravenously.

MAJOR GERARD DE ORO, MC, AUS. Could she not just take thiamine hydrochloride by mouth?

DR HARRY L. ARNOLD JR. Dr. Badger, who did a good deal of work on this disease at Kalaheo Hospital a few years ago, obtained much better results with large doses given intravenously.

#### Nevus Unius Lateris Presented by DR HAROLD M. JOHNSON

M. T., a 28 year old Japanese man, presents a line verrucous zosteriform lesion on the right lower part of the abdomen, extending to the umbilicus and radiating in a verrucous linear pattern to the right groin and down the right leg in the distribution of the sciatic nerve. There are no symptoms. A sister has a port wine nevus on the entire right side of her face and temporal area. A cousin has a lesion like the patient's. The patient's daughter also has a port wine nevus on the left forearm.

#### Lichen Striatus Presented by DR HAROLD M. JOHNSON

D. K., a 7 month old boy, suddenly had a flesh-colored verrucous linear dermatosis of the entire left half segment of his body about one and one-half months ago. The child has been well, without any predisposing infection. There was no other family history involved.

The lesions are verrucous and patchy or grouped at certain locations on the scalp, the left side of the face, the chest and the back. There are several long linear plaques running across the abdomen and back in the

iform arrangement. The lesions completely cover the buttock and follow the distribution of the great saphenous nerve to the mesial aspect of the left plantar surface of his foot. The lesions have improved and are not as elevated or verrucous as before. Some of the lesions have a lichenoid appearance resembling that of lichen planus. The right side is completely clear of any lesion except the scars of recent chickenpox.

#### DISCUSSION OF THE TWO PRECEDING CASES

DR HARRY L. ARNOLD JR. I should have thought that both of these cases were examples of nevus unius lateris, except for the recent onset and apparent beginning involution.

DR HAROLD M. JOHNSON. The child's lesion appeared almost overnight and is now disappearing, after being present for only about six weeks. This is the typical course of lichen striatus, according to Senechal.

LIEUT. HARRY KATZ, MC-V(S), USNR. What is the prognosis of lichen striatus? Do these lesions disappear entirely?

DR HARRY L. ARNOLD JR. I saw lesions precisely like that of the man in a tuberculous patient at Lehigh some a couple of years ago, and they disappeared completely in a few months.

MAJOR ALBERT SHAPIRO, MC, AUS. I think that with the clinical course and the lichenoid appearance of the individual papules are practically diagnostic of lichen striatus in the first case.

#### Morphea-Like Basal Cell Epithelioma with Ulceration

Presented by DR HAROLD M. JOHNSON

P. A., a 35 year old member of the Army Transport Command, presented a small papule in his right temporal area, first noticed about three years ago. The lesion has been excoriated many times in the interim. The lesion has increased several times in size during the last year. The patient has been exposed to a considerable amount of sunshine during the last year, on one occasion he spent sixteen days in a lifeboat on the Atlantic Ocean after his ship was torpedoed. Army and Navy medical officers told the patient that the lesion was a tropical ulcer or low grade bacterial infection. Many remedies have been used, including ointments and internal medication. The patient's grandfather and grandmother had carcinoma, and two uncles had epithelioma of the skin.

The lesion is an irregular-shaped ulcerated surface, about the size of a half-dollar, located in the right temporal area. There are no glands palpable.

#### DISCUSSION

DR HAROLD M. JOHNSON. If biopsy shows a basal cell epithelioma, I shall refer the patient for excision and plastic repair.

CAPT. L. H. ROSENTHAL, MC, AUS. Why not roentgen ray therapy?

DR HAROLD M. JOHNSON. I do not believe that morphea-like basal cell epitheliomas are radiosensitive.

CAPT. L. H. ROSENTHAL, MC, AUS. I do not think that an ulcerated basal cell lesion like this one could be classified as morphea-like. Morphea-like epitheliomas have a waxy, indurated, scleroderma-like surface.

DR HAROLD M. JOHNSON. In any case the patient is traveling constantly and cannot have regular roentgen treatments or dressings following coagulation.

NOTE.—Biopsy showed a morphea-like basal cell epithelioma.

#### Atypical Miliaria

Presented by CAPT. HERBERT LAWRENCE, MC, AUS

F. B., a 25 year old former bricklayer, presented a scaly erythematous pruritic eruption in both cubital and popliteal areas. It first appeared about ten years ago during the summer. Since then it has always recurred in the summer and has spread to involve most of the trunk, arms and legs in a strangely circumscribed fashion. During the winter the eruption would subside but would not completely disappear. There is no family history of allergy nor any history of hay fever, asthma or eczema. The patient has been in the Aleutian Islands, and there was virtually no evidence of the eruption while he was there. Soon after his arrival in the semitropics the eruption relapsed, and it has become progressively worse. On several occasions he has been hospitalized and all evidence of the eruption almost eradicated with cooling compresses and lotion. However, the eruption has reappeared when the patient returned to duty. The eruption has always been worse in intertriginous areas, and at times it has become acutely inflamed and weeping and finally erosive.

The same areas are always involved, and in addition, from time to time, the eruption has started at new sites. Areas of involvement at present are the outer margins of both axillae. Usually the axillae themselves are clear, although at present the left axilla is involved. Both cubital areas are involved, with extension from them along the anterior aspects of both arms. There is an irregular "splotchy" area of involvement of most of the anterior part of the trunk and similar involvement on the lower portion of the back and left thigh. The eruption is characterized by erythematous follicular papules, most of which have coalesced to form huge plaques. Some of the plaques have an arciform appearance, the concave aspect of which shows a residuum of desquamation and brownish pigmentation. The skin in the cubital area has become secondarily thickened and lichenified.

Histologic section showed a perivascular round cell infiltration in the cutis.

#### DISCUSSION

CMDR. GEORGE C. DOYLE, MC-V(S), USNR. My first impression in this case was that the disease is an unusual variant of atopic eczema.

DR. JAMES T. WAYSON. I thought that the history and the appearance of the eruption suggested atypical lichen planus.

MAJOR ALBERT SHAPIRO, MC, AUS. I think that the disease looks more like atopic dermatitis because of the lichenification and confluence of the lesions. Miliaria rarely becomes confluent.

CAPT. HERBERT LAWRENCE, MC, AUS. I am convinced that this eruption is representative of the clinical picture known as miliaria ("prickly heat"). It is merely more extensive and chronic. This is the third such case I have seen in Hawaii, and no doubt the climate is responsible for the severity of the eruption.

#### Nevus Pigmentosus et Verrucosus

Presented by CAPT. HERBERT LAWRENCE, MC, AUS

S. R., a 25 year old man, who had previously been a farmer, has had since birth a pigmented papillomatous lesion in the left pectoral region. It had not enlarged or in any way altered in appearance until about January 1944. At this time the patient noticed a brownish discoloration at the periphery of the lesion. He is sure

that this had never been present before. The lesion itself has not changed. There is no history of traumatization or unusual exposure to the sun, although the patient's arrival in this locality was concomitant with the changes around the lesion.

In the left pectoral region there is an oval lesion, sharply circumscribed but with a serrated peripheral border, giving the impression of small blunt projections along the border. The peripheral quarter of the lesion is flat and brownish black and contains normal lanugo hairs. The central portion of the lesion is papillomatous and brownish black and contains long hairs. There is a zone of light brown pigmentation scattered irregularly about the periphery of the lesion. Some of the pigmentation has coalesced to form confluent areas, but there are also areas of pinhead-sized pigmented macules. As far out as the right border of the sternum, approximately on the level of the lesion itself, there is sparsely scattered light brown pigment. Just above both clavicles there can be felt elongated cordlike lymph nodes, slightly larger on the left side. No axillary adenopathy is felt.

## DISCUSSION

CAPT L H ROSENTHAL, MC, AUS. I think that this is a definitely benign lesion which should be excised because it is unsightly and annoying to the patient.

CAPT HERBERT LAWRENCE, MC, AUS. I plan to excise it widely, including the rather widespread pigmentation about the main body of the lesion.

DR HAROLD M JOHNSON. Personally I should be reluctant to do this. There is always the possibility of stirring up something by such a procedure.

DR HARRY L ARNOLD JR. If one gets into trouble after excising a lesion, the lesion was already malignant, removing it did not make it so. I would excise it without hesitation.

LIEUT HARRY KATZ, MC-V(S), USNR. So would I. The patient would like to have it removed, and I see no contraindication to excising it, if only for cosmetic reasons.

CAPT HERBERT LAWRENCE, MC, AUS. It seems to me that the recent appearance of new pigment around any pigmented nevus should be regarded as a criterion of progression and as highly suggestive of malignant degeneration.

DR HARRY L ARNOLD JR. Has this man not been getting more sunshine on his chest since coming to Hawaii?

CAPT HERBERT LAWRENCE, MC, AUS. It is true that the new pigmentation has developed since he came here.

DR HARRY L ARNOLD JR. There is one other possibility. I have been impressed with the frequency with which, in persons coming to Hawaii for the first time, mild hypothyroidism develops soon after their arrival. Possibly enough thyroid depression has developed to stimulate his pigment-producing mechanism.

NOTE—The lesion was widely excised and proved to be a pigmented cellular nevus of junction type with abundant hyperkeratosis.

**Lupus Erythematosus Disseminatus (Response to Sulfadiazine?)** Presented by DR HARRY L ARNOLD JR.

G V, a 22 year old Caucasian housewife, was first seen on April 10, 1944, because of migratory arthritis and an urticaria-like eruption associated with moderate

fever, malaise and a loss of 10 pounds (4.5 Kg) over a period of five months.

The eruption was simply papular erythema multiforme both clinically and histologically. Leprosy was excluded by the absence of thermal anesthesia and by the histologic changes. There was leukopenia. The urine was normal, the sedimentation rate was 49.5 per cent (normal 1 to 5 per cent), and the Weltmann reaction was 8 (modified Westergren). The heterophile antibody reaction was negative.

Three weeks later the patient was worse. The spleen was palpable, the serum proteins were 7.47 Gm per hundred cubic centimeters, with an albumin-globulin ratio of 0.9, the Weltmann reaction was 8.5, and the Mantoux reaction was negative. A roentgenogram of the chest showed only generalized exaggeration of vascular markings. The sputum and the urine were normal.

After one week of treatment with sulfadiazine with a blood level of 9.2 mg per hundred cubic centimeters she was much worse, the eruption more severe, the temperature 102 F and the white blood cell count down to 3,000, there was also generalized lymphadenopathy. The drug was stopped, and the patient promptly recovered, the skin cleared, the spleen was no longer palpable, the temperature returned to normal, and the white blood cell count returned to 5,250 with 70 per cent neutrophils.

Ten days later the eruption was beginning to return, and the spleen was again palpable.

## DISCUSSION

DR HARRY L ARNOLD JR. The Weltmann reaction in this patient is not of the type one would expect in a patient with such extensive exudative disease, it was shifted to the right instead of to the left and has remained so. The sedimentation rate was very high. These two tests ordinarily have an inverse relationship. The apparent flare-up from sulfadiazine was interesting. Dr Johnson had previously suggested to me that eradication of foci of infection by sulfonamide compounds, like their surgical eradication, may be accompanied with a Herxheimer reaction before the ultimate clinical improvement. Certainly this patient's course would be explained by such a hypothesis.

DR HAROLD M JOHNSON. It seems to me that penicillin should be valuable in at least some cases of lupus erythematosus disseminatus.

DR HARRY L ARNOLD JR. Dr Chester Keefe assures me that it has been tried and has failed. Has any one seen this peculiar injection of the temporal portion of the bulbar conjunctiva of one eye in a patient with disseminated lupus erythematosus?

NOTE—The patient subsequently had a severe exacerbation from sulfamerazine, followed by transient recovery and a second gradual relapse. Penicillin (only 200,000 units in forty-eight hours) subsequently produced only slight and transient benefit.

Larger doses later had no effect. The patient had gradually become worse, though the urine has remained normal. Slow but steady improvement has been noted since October 1945, when semiweekly injections of staphylococcus antitoxin were begun.

**Tropical Ulcer** Presented by MAJOR GERARD DE ORO and CAPT L H ROSENTHAL, MC, AUS.

R J S, 34 years old, suffered a slight abrasion on the left shin three and one-half months ago. Shortly afterward, a small pustule appeared at the site and

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developed into an ulcer, which grew rapidly. Two weeks later an ulcer appeared on the right shin, followed by the appearance of two small ulcerations distally on the leg. The ulcer on the left leg became granulomatous, and the three ulcerations on the right leg continued to grow with development of moderate granulation tissue.

The patient was admitted to the hospital two months ago. The ulcer on the left leg measured 4 by 2 inches (10 by 5 cm), was oval in outline and presented a grossly granulomatous surface with a slightly elevated demarcated border. The three ulcers on the right leg were in linear arrangement, varying from 2 to 1 inch (5 to 2.5 cm) in diameter, and presented a punched-out appearance, with some areas showing granulomatous tissue. Treatment resulted in the disappearance of the granulomatous features and all of the surrounding erythema and edema. The borders are no longer elevated or edematous. The base of each is erythematous and free of discharge and appears to be healthy granulating tissue. However, the ulcers are slow in healing.

Biopsy showed chronic inflammation of a nonspecific variety. The blood counts, urinalyses and roentgenograms of the bony structure of the legs were normal. The sedimentation rate increased from 60 to 110 mm in sixty minutes. Culture of the wound repeatedly yielded *Bacillus pyocyaneus* and hemolytic staphylococci. There was no evidence of sickling of the red cells. Examination of the stool revealed normal conditions.

Treatment consisted of sulfonamide compounds internally or locally for six weeks, packs of boric acid, potassium permanganate, mercury bichloride and aluminum acetate solutions, ammoniated mercury ointment (5 per cent), injections of staphylococcus toxoid and weekly roentgen irradiations (75 r) for ten weeks.

## DISCUSSION

MAJOR GERARD DE OREO, MC, AUS. I think that the terms "tropical ulcer," "desert sore," "Barcoo rot" and so on are all misleading, because they pretend to designate a specific entity. I think that this lesion is a nonspecific ulceration due to mixed bacteria, with occasionally a fusospirochetal component, occurring in warm humid climate, which helps these mixed organisms to grow, thereby favoring a chronic resistant erythema-like process.

MAJOR ALBERT SHAPIRO, MC, AUS. Although many different types of ulcerative processes of the skin may be encountered, there is one form of ulceration known as tropical ulcer which is regarded by many as a definite clinical entity. The diagnosis is made by finding large numbers of fusiform bacilli and spirochetes morphologically identical with the *Spirochaeta vincenti* both on smears and throughout the tissue on biopsy. Because of the absence of these organisms and the presence only of *B. pyocyaneus* and hemolytic staphylococci, I should classify this case as one of pyogenic ulcerations.

DR HAROLD M. JOHNSON. I should think that penicillin either locally or parenterally would be the ideal treatment for these lesions, whether they are a spirochetosis or not.

MAJOR GERARD DE OREO, MC, AUS. Dr. John Devine, in Australia, has reported a large series of cases of tropical ulcer in which he found no higher incidence of spirochetes than in any other similar lesions. He found that any hygienic measures would promote healing.

## "Neural" (Early Tuberculoid?) Leprosy Presented by DR HAROLD M. JOHNSON

J. S., a 30 year old part Hawaiian housewife, consulted her private physician in July 1944 because of acute paronychia of the right first toe. The physician's suspicions were aroused by the apparent and inconsistent painlessness of the lesion, and he referred her to me.

There were tactile and thermal anesthesia of the right foot. The posterior tibial and sural nerves were enlarged and tender at the point where they passed behind and below the malleoli at the ankle. On the forearms she had several hypopigmented macules, from 2 to 10 cm in diameter, which were anesthetic to heat and cold although not to touch.

Biopsy of the anesthetic portion of the foot revealed only slight, nonspecific perivascular inflammation without acid-fast bacilli. A biopsy specimen from a macule on the left forearm showed perivascular lymphocytic and epithelioid cell infiltration, which was regarded as compatible with extremely early changes of tuberculoid leprosy, a few acid-fast bacilli were found.

The patient was referred in the usual manner to the Kuku Street Leprosy Clinic, where these findings were confirmed and, in addition, a scraping of the nasal septum was made. This specimen contained numerous acid-fast bacilli in clumps and globi. This was regarded as a highly inconsistent finding, however, because of the type of leprosy which the patient had, and the scraping was therefore repeated forty-eight hours later on both sides of the septum. Both preparations this time showed no acid-fast bacilli whatever. The patient was accordingly legally declared a leper by a board of three physicians and was recommended for immediate temporary release, with instructions to report once a month for a check-up examination at the clinic. She was sent back to her original physician for intravenous injections of thiamine hydrochloride for the relief of pain and tenderness in the involved nerve. This subsided completely after a week or ten days.

## DISCUSSION

DR HARRY L. ARNOLD JR. This case would be officially classified as one of neural leprosy, Na 1, Ns 1. These symbols mean, respectively, neural-anesthetic, minimal degree, and neural simple macular, minimal degree. The former expression ("anesthetic") refers to the involved nerves and anesthetic skin of the foot, and the latter ("simple macular"), to the hypopigmented macules, or, as the leprologists call them, "simple macules," on the forearms.

DR HAROLD M. JOHNSON. Is that classification accepted now?

DR HARRY L. ARNOLD JR. Yes, it has been official since the 1938 International Conference, at Cairo, Egypt.

DR JAMES T. WAYSON. These standard classifications are all right for a small group like this one but not for general use, when a case is written up and these symbols are used, a physician who has not seen the case cannot tell a thing about it.

DR HARRY L. ARNOLD JR. I think that that is an excellent point. Dr. Tilden and I have recently been concerned with the confusion that surrounds the classifications of leprosy, and we have attempted to clarify it a little (The Two Kinds of Leprosy: Lepromatous and Tuberculoid, *Proc. Staff Meet., Clin., Honolulu*, 10:91 [Sept.] 1944, and The Classifications and Nomenclature of Leprosy, *Ann. Int. Med.* 23:65 [July] 1945).

This case would be classified by Pardo-Castello and his group as "leprosy of the skin, simple inflammatory, and leprosy of the nerves, type undetermined but presumably simple inflammatory or tuberculoid" Dr Tilden and I feel that a case like this is so likely to become an outspoken example of tuberculoid leprosy and so unlikely to become a case of lepromatous leprosy that it is more informative to classify it at the outset as "early tuberculoid" leprosy I should like to ask Dr Wayson whether he thinks a case like this is likely ever to become a heavily positive lepromatous case

DR JAMES T WAYSON I think that the chances are 1 in 100 A patient like this presents no danger to the public or to people living in the same house with her I have always recommended paroling such patients and sometimes even overlooking them as far as official recognition is concerned

DR HARRY L ARNOLD JR I should like to emphasize another instructive feature about this case, namely, the presence of organisms in nasal scrapings which I obtained at the Kukui Street Leprosy Clinic It seems to me that if the organisms found there were *Mycobacterium leprae* we should have been able to find a few of them on at least one side of the septum forty-eight hours later The fact that we found none strongly suggests to me that these were superficial saprophytic acid-fast diphtheroid bacilli, which she just blew out of her nose between the first and second examinations I should like to have Dr Wayson's opinion about this, as well

DR JAMES T WAYSON I should think that leprosy bacilli in a patient's nose would still be found there forty-eight hours later There are many acid-fast bacilli that can be found in the nose that are not *Mycobacterium leprae*

DR HARRY L ARNOLD JR I am glad to hear you say that It is my own feeling that examination of nasal scrapings is not worth the trouble for diagnostic purposes because the results are inconclusive if negative and may be misleading if positive

#### Late Cutaneous Syphilis (Gumma) with Negative Serologic Reactions Presented by DR HAROLD M JOHNSON

M M, a 70 year old retired Japanese man, was first seen on Sept 7, 1944, because of an indurated circinate plaque on the lateral aspect of the right knee with scarring in the center The scar was smooth and flexible and not contracted The plaque itself appeared granulomatous, with a verrucous surface There was a similar plaque, somewhat arciform in configuration, on the mesial side of the knee Both lesions began four or five years ago and have slowly increased in size, without any tendency to spontaneous healing The remainder of the physical examination revealed no abnormalities

A complete blood count and a urinalysis showed normal conditions A roentgenogram of the chest showed no pulmonary disease Serologic tests for syphilis (Wassermann and Kahn) elicited negative reactions on two occasions at Queen's Hospital and the Board of Health laboratory

A biopsy specimen from the border of the lesion showed only a dense, almost purely lymphocytic infiltrate just beneath a slightly acanthotic epidermis and extensive replacement of the normal collagen by young fibrous tissue The disease was reported as chronic infectious granuloma of uncertain cause

#### DISCUSSION

DR HAROLD M JOHNSON Clinically, I was led to think of either tertiary syphilis or lupus vulgaris, more likely the former

DR HARRY L ARNOLD JR The relatively long duration led me to think that the disease was more like lupus vulgaris I have seen very few cases of seronegative cutaneous syphilis

CAPT L M ROSENTHAL, MC, AUS I made diagnosis of late syphilis for this man, notwithstanding the five years' duration and the negative serologic reactions I think that the thin noncontractile central scar is strongly in favor of a diagnosis of late syphilis as opposed to that of tuberculosis

MAJOR SOLOMON GREENBERG, MC, AUS Yes, the serologic reactions may be negative in 45 or 50 per cent of cases of late cutaneous syphilis

DR HAROLD M JOHNSON A trial of a water-soluble bismuth preparation should settle the question conclusively

NOTE—The lesion cleared about 75 per cent after six semiweekly injections of bismuth and potassium tartrate

#### Sporotrichosis Presented by DR HAROLD M JOHNSON

P C, a 33 year old Filipino plantation laborer, was first seen on Sept 8, 1944, with a history of suppurative lesions of about three months' duration on the left arm The initial lesion had been treated as a boil, but when a series of lesions subsequently developed along the same arm, each one proximal to the last, following the mesial lymphatic drainage the patient was referred for further study Blood counts were within normal limits Serologic tests for syphilis elicited negative reactions A roentgenogram of the chest revealed no abnormalities and the Mantoux test elicited a negative reaction

The lesions did not respond at all to sulfanilamide or sulfathiazole applied locally or given internally Penicillin-inoculated gauze dressings locally had no effect

#### DISCUSSION

CAPT HERBERT LAWRENCE, MC, AUS Does one see many cases of sporotrichosis in Hawaii?

MAJOR SOLOMON GREENBERG, MC, AUS I have seen 1, the patient being a soldier in the ward in whom the disease developed after he had pricked his finger with a thorn

DR HARRY L ARNOLD JR I had 1 proved case, of the ulcerative type, five years ago

DR HAROLD M JOHNSON I have seen 3 cases in the last two years

MAJOR SOLOMON GREENBERG, MC, AUS In the 1 case which I saw the patient was given potassium iodide and the disease cleared promptly

DR HARRY L ARNOLD JR I have seen 2 patients with gummatous sporotrichosis cured rapidly with potassium iodide I wonder whether penicillin is effective against *Sporotrichum schenckii*, as it is supposed to be against *Actinomyces*

CAPT L H ROSENTHAL, MC, AUS It has no effect on blastomycosis

NOTE—The cultures showed *S. schenckii* after fourteen days on Sabouraud's medium

#### A Case for Diagnosis (Keratosis Palmaris?) Presented by DR HARRY L ARNOLD JR

D E H, a 17 year old white war worker, was first seen in August 1944, because of roughly symmetrical



4 tremely heavy calluses, irregularly distributed over both palms. They had been present for about two years. Evidently, according to the patient, did not develop during a period of particularly heavy manual work. They had occasionally been a little painful, especially in the mornings. No biopsy was made, and no laboratory studies were undertaken.

## DISCUSSION

MAJOR L. H. ROSENTHAL, M.C., A.U.S. I think that the growths are a form of keratosis palmaris, despite the recent onset and the lack of involvement of the feet. I should regard it as a nevroid disease. I think that it would be unlikely to respond, except temporarily, to any treatment.

DR JAMES T. WAYSON. I suggest a 50 per cent salicylic acid ointment used as frequently as necessary.

**Epidermolysis Bullosa Acquisita Complicated by an Annular Vegetative Iododerma** Presented by DR HARRY L. ARNOLD JR.

MR. O., a 74 year old Puerto Rican laborer, was first seen on Sept. 4, 1944, because of two eruptions. One had been present at intervals for four or five years and consisted of blackish ill defined scaly macules and scars on all the knuckles of both hands, on both feet and on a few other bony prominences of the extremities. These were said by his physician to have followed recurrent vesicular lesions in these locations.

The other eruption was of only two weeks' duration, consisted of red annuli, 2 to 10 cm in diameter, with raised, cordlike edges, about 2 mm wide, scattered principally over the arms and legs and the upper part of the back, on the back they were much more elevated and vegetative in appearance and in some areas were fluctuant and even suppurating. The face and scalp and the eyelids were the sites of multiple small nodules and tumors, from 2 to 10 mm in diameter, that had appeared at the same time as the annular lesions and were more vegetative and suppurative than annular. The pus was sterile on culture. The mucous membranes were spared, and the palms and soles were free except for a single annulus in one palm. These lesions had all appeared when the patient began taking potassium iodide, in the county convalescent home.

Examination otherwise disclosed nothing significant except for a positive serologic reaction for syphilis, a widening of the supracardiac shadow in a roentgenogram of the chest and a hemoglobin content of only 7 Gm per hundred cubic centimeters.

Biopsy of a flat annulus on the thigh revealed only mild nondescript inflammatory changes in the corium, sections from a vegetative annulus on the arm showed profuse infiltration by a mixed cellular infiltrate consisting chiefly of polymorphonuclear leukocytes, with an admixture of lymphocytes, histiocytes, fibroblasts, plasma cells, mast cells and eosinophils, the last three in small numbers only. Stains for elastic tissue did not show significant reduction of elastic fibers in the subpapillary layer. (Such a reduction was later demonstrated, though it was not striking, in a biopsy specimen of a hemorrhagic bulla over one internal malleolus.)

## DISCUSSION

DR HAROLD M. JOHNSON. This man was seen at the Alabama Clinic in 1942 with an annular iododerma.

CAPT L. H. ROSENTHAL, M.C., A.U.S. If this eruption is epidermolysis bullosa, it had its onset at the most advanced age of any that I have ever heard of.

CAPT HERBERT LAWRENCE, M.C., A.U.S. The appearance of the deeply pigmented lesions on the bony prominences of the hands and feet made me think of Kaposi's sarcoma, and I still think that the general appearance is consistent with that diagnosis.

DR IRVIN L. TILDEN (by invitation). The histologic changes are not inconsistent, either.

CAPT DAVID MUSMAN, M.C., A.U.S. Does the patient have any past history of venereal disease?

DR HARRY L. ARNOLD JR. He has syphilis, for which he has been treated.

CAPT DAVID MUSMAN, M.C., A.U.S. I thought that he might have keratosis blennorrhagica.

MAJOR SOLOMON GREENBERG, M.C., A.U.S. The eruption did not look like that to me. Keratosis blennorrhagica shows heaped-up oystershell crusting, which this man did not have.

CAPT L. H. ROSENTHAL, M.C., A.U.S. The picture might be unified, perhaps, by regarding these lesions on the bony prominences as similar to the joint-articular nodes of syphilis.

**Lichen Sclerosus et Atrophicus** Presented by DR HARRY L. ARNOLD JR.

MS., a 49 year old Caucasian housewife, was first seen on Sept. 7, 1944, because of an asymptomatic eruption confined to the trunk, first noticed about a year before. Six or eight oval atrophic slightly depressed hypopigmented macules, covered with thin lamellar scale and measuring 1 to 2 cm in diameter, were scattered over the upper portion of the trunk, and some forty or fifty similar but much smaller lesions, measuring 1 to 5 mm in diameter, were grouped within a palm-sized area on the small of the back. There was no follicular dilatation or plugging. The remainder of the cutaneous surface was spared, and the mucous membranes were normal.

The white blood cell count was 9,200 per cubic millimeter, with 70 per cent polymorphonuclear cells and 3 per cent eosinophils. Serologic tests for syphilis elicited negative reactions.

Biopsy showed a remarkable degree of edema of the papillary and subpapillary layers of the corium, with extraordinary dilatation of lymphatic spaces, a few of which contained pink-staining coagulated material and much interstitial edema fluid as well, the neighboring collagen was "homogenized" in appearance. The overlying epidermis was atrophic, with loss of rete pegs, and hyperkeratotic. There was no evidence of follicular dilatation or plugging.

## DISCUSSION

CAPT HERBERT LAWRENCE, M.C., A.U.S. I think that it is most unusual to see lesions so numerous and so widespread in a case of lichen sclerosus et atrophicus.

CAPT DAVID MUSMAN, M.C., A.U.S. Were lesions present on the scalp? I did not want to muss the patient's hair.

DR HARRY L. ARNOLD JR. I regret to confess that I did not examine her scalp. The literature in the past has suggested some disagreement as to whether the change in the upper part of the corium consists in part or in entirety of edema. I think that in this case there can be no question that there is abundant edema, some of it in the collagen and some of it in greatly dilated lymphatic spaces.

NOTE.—The lesions healed, leaving faint scars, after twelve weekly intramuscular injections of bismuth subsalicylate in oil, 0.2 Gm each.

### A Case for Diagnosis (Poikiloderma?). Presented by DR HARRY L ARNOLD JR

C G, a 49 year old Caucasian housewife, was first seen on Aug 17, 1944, because of a two year old eruption confined to the sides of the neck posteriorly, first on the right and more recently on the left, consisting of imperfectly discrete erythematous macules a few millimeters in diameter, without dyspigmentation, atrophy, scaling, telangiectasia or pruritus. There has been no perceptible spreading in the past six months.

No special studies have been undertaken.

#### DISCUSSION

CAPT HERBERT LAWRENCE, MC, AUS I thought of the possibility of a berlocque dermatitis.

CAPT L H ROSENTHAL, MC, AUS I agree with the diagnosis of poikiloderma of Civatte. I think that the patient will eventually show some atrophy and pigmentary changes.

CAPT DAVID MUSMAN, MC, AUS I thought of the possibility of a contact dermatitis. The patient admitted readily that she used "just a very little" rinse once in a while on her hair.

DR HARRY L ARNOLD JR I was reluctant to make a diagnosis of poikiloderma of Jacobi without any telangiectasia or atrophy or of poikiloderma of Civatte without any pigmentary changes.

### Alopecia Totalis Associated with Onychodystrophy Presented by CAPT HERBERT LAWRENCE, MC, AUS

A 40 year old white man was first seen a few days ago, because of total loss of hair. This had begun in a circumscribed patch on his right cheek about December 1943 and had progressed to a total loss of every hair on the entire body, including the eyelashes and the hair on the extremities. At about the time when this became complete, that is, in March 1944, the finger nails and the great toe nails began to be ridged longitudinally and to be opaque and brittle, this has continued until the entire length of all the finger nails and the great toe nails is so involved.

#### DISCUSSION

MAJOR SOLOMON GREENBERG, MC, AUS Do you know what the basal metabolic rate is?

CAPT HERBERT LAWRENCE, MC, AUS It has not been determined, but the patient's weight has not changed, his skin is not dry, and he does not complain of symptoms of hypothyroidism.

MAJOR SOLOMON GREENBERG, MC, AUS I had a soldier in the ward almost totally devoid of hair, with an only slightly lowered basal metabolic rate, who recovered all his hair after being given some thyroid. I do not say that the thyroid cured him, but at least he got well after taking it.

DR HARRY L ARNOLD JR I have seen 2 cases of alopecia totalis in which I have tried the effect of a single epilating dose of roentgen rays to the back of the scalp. It had no effect whatever in either case. I have never seen this or any other sort of onychodystrophy in association with alopecia. I should be inclined to suggest psychiatric investigation of these cases rather than the usual blind administration of endocrine substances.

CAPT HERBERT LAWRENCE, MC, AUS It has seemed to me that this man takes his disease lightly. He says that it does not bother him at all, in fact, he enjoys not having to shave or brush his hair.

### Generalized Progressive Scleroderma with Raynaud's Syndrome Presented by DR HARRY L ARNOLD JR

E B, a 24 year old Portuguese housewife, was first seen on Aug 11, 1944, because of progressive hardening and tightening of the skin over a period of about three years. It had first been called to her attention by a masseuse in 1941. After the onset of the war, in December of that year, she went to San Diego, Calif., and soon after arriving there she began to have pallor and pain in her fingers on exposure to cold, little indolent ulcers also developed on her finger tips from time to time. Shortly afterward she became aware that the tightening of her skin was progressing and was beginning to be associated with a bronzelike pigmentation on the face, hands and arms. On her return to Hawaii in 1943 the painful vasospasm in her hands practically stopped, being brought on only by contact with cold water or other cold objects. The hardening of the skin continued to progress.

On examination she showed abnormally thin tight, bronzed skin on the hands, arms, face, neck and upper part of the chest. The finger tips showed a few small scars. The skin was otherwise normal. The dorsalis pedis arterial pulse was well felt bilaterally. The blood count showed mild hypochromic anemia and the presence of 16 per cent monocytes, serologic tests for syphilis elicited negative reactions, and urinalysis revealed normal conditions. The basal metabolic rate was +18 per cent (adjusted for Hawaiian normal standards, +27 per cent) the pulse rate was 90, cooperation was good. The serum cholesterol level was only 40 mg per hundred cubic centimeters (normal, 150 to 220 mg), and on recheck three weeks later it was only 32 mg. The Weltmann coagulation band was 9—a pronounced shift to the right—and the sedimentation rate was 37 per cc (74 mm per hour). The serum proteins were 7.38 Gm per hundred cubic centimeters, of which 4.16 Gm was albumin and 3.22 Gm was globulin, a ratio of 1.3:1.

A surgical consultant recommended lumbar sympathectomy and, later, if the response justified it, cervical sympathectomy as well.

#### DISCUSSION

DR HARRY L ARNOLD JR This case presents two particularly interesting features. One of them hinges on the fact that Raynaud's syndrome is almost never encountered in Hawaii, and this patient had no symptoms of the syndrome until she was exposed to the winter climate of San Diego in 1941. Lieut Comdr Werner Duemling saw her at that time and made the diagnosis. Since her return to Hawaii she has had only Raynaud symptoms except on touching cold water or cold objects.

The other interesting feature of the case is the rather spectacular aberrations of the blood chemistry which she presents. Aside from the suggestion of hyperparathyroidism and an elevated blood calcium level which appears to be a feature of ordinary scleroderma, changes in blood chemistry do not appear to have been found in cases of scleroderma. This woman has a serum cholesterol level which is between a fourth and a fifth of the minimum normal value, a hyperglobulinemia and a decided shift of the Weltmann band to the right. The sedimentation rate, interestingly, is elevated, instead of being low, as is usually the case when the Weltmann band is shifted to the right. The combination of a shift to the right of the Weltmann band, a high sedimentation rate and a low serum cholesterol level also appears to occur in at least some cases of subacute disseminated lupus erythematosus.



DR IRVIN L TILDEN (by invitation) I have never even a Weltmann coagulation band higher than 9, and see only coagulation bands of 9 that I ever saw prior to this one were in cases of cirrhosis of the liver

DR HAROLD M JOHNSON Have you made a determination of calcium-phosphorus balance?

DR HARRY L ARNOLD JR No, we have not

DR HAROLD M JOHNSON Bismuth hydroxide is being used for scleroderma I believe that the dose is similar to that of bismuth subsalicylate

DR HARRY L ARNOLD JR I should like to ask Dr Wayson if he has ever seen a case of either scleroderma or acrosclerosis in Hawaii

DR JAMES T WAYSON I do not recall that I ever give, except for 1 case in which there were numerous circumscribed hardenings of the skin

NOTE—Bilateral lumbar sympathectomy on Sept 19, 1944, and cervical sympathectomy on Feb 8 and Sept 1945 resulted in complete relief of the Raynaud symptoms but did not affect the slow progression of the scleroderma Dysphagia began in April 1945

**Case for Diagnosis (Dermatitis Herpetiformis?)**  
Presented by DR TAKEO FUJII (by invitation)

DR I, a Japanese girl 11 months old, was first seen in August 1944, because of a generalized vesicular eruption which had appeared two weeks before, immediately following a circinate macular rash, associated with fever and a running nose, which was thought to be measles. The vesicles ranged from 2 or 3 mm to 2 cm in diameter and were filled with clear fluid. The only areas spared were the back, from the shoulders to the buttocks, and the mucous membranes. The child had had chickenpox in May but had otherwise been in good health. There was a leukocytosis with a count of 11,000 cells, with 5 per cent eosinophils, and the vesicle fluid showed about 5 per cent eosinophils. A culture from a vesicle showed a few colonies of Staphylococcus aureus. There was no history of an allergic familial background.

The baby was hospitalized and given sulfathiazole and improved steadily after the dose had been sufficiently increased (to 0.5 Gm six times a day) to maintain the blood level at about 5.9 mg per hundred cubic centimeters. The lesions did not completely clear, however, and when the dose was raised to 1 Gm every four hours the baby had an attack of syncope from which she had to be revived by artificial respiration. The sulfathiazole level of the blood at this time was 14.8 mg per hundred cubic centimeters. After sulfathiazole was not given for three days the lesions recurred. The patient was then given penicillin intramuscularly, 10,000 units every four hours for three days, during which time the white blood cells count remained around 18,000 cells per cubic millimeter and the eosinophils around 15 per cent. The lesions did not respond. After this penicillin and sulfathiazole was given, also without effect. All medication was discontinued for three days before her presentation today, and the white blood cell count today was 11,000 with 13 per cent eosinophils.

**DISCUSSION**

DR HAROLD M JOHNSON I first saw this patient when she was in the Kaulaolani Children's Hospital, and at that time she had an extensive impetigo, which I thought was the primary diagnosis. I now feel that this was secondary to dermatitis herpetiformis. I agree with the diagnosis as presented.

DR JAMES T WAYSON What about sensitivity to iodides?

DR HARRY L ARNOLD JR There is not a large enough area of normal skin on this baby now to permit a patch test with potassium iodide, and the continuous activity and severity of the disease have prevented testing for sensitivity to iodides by the oral route.

CAPT L H ROSENTHAL, MC, AUS I notice that sulfapyridine has not been tried, it is my impression that that is the sulfonamide compound of choice for this disease.

DR HARRY L ARNOLD JR That is the consensus in the literature. My own experience is that sulfathiazole is just about as effective and a good deal less likely to produce reaction.

CAPT L H ROSENTHAL, MC, AUS I wonder whether a test for allergy has been given here—an elimination diet, for example.

DR TAKEO FUJII (by invitation) Yes, the baby was tried on a diet of water for twenty-four hours followed by the addition of one food at a time. There was no change in the eruption during this period.

CAPT HERBERT LAWRENCE, MC, AUS If this eruption is indeed dermatitis herpetiformis, this is the third infant I have seen with the disease in a single year. I think perhaps many of us are not accustomed to thinking of dermatitis herpetiformis as an affliction of infants.

DR HAROLD M JOHNSON What history is there of allergy in the family?

DR TAKEO FUJII (by invitation) The father gets an eruption of some sort from alcoholic beverages, and an uncle gets angioneurotic edema after he drinks a glass of beer. The mother thought that the baby was sensitive to orange juice, but I have not been able to confirm this.

DR HARRY L ARNOLD JR I think that the failure of penicillin in adequate dosage to affect this patient is extremely interesting. I had supposed that penicillin would help in most, if not in all, cases of dermatitis herpetiformis.

**LOS ANGELES DERMATOLOGICAL SOCIETY**

WILLIAM H GOECKERMAN, MD, *Chairman*

CLEMENT E COUNTER, MD, *Secretary*

June 13, 1944

**Chloasma Uterinum** Presented by DR H C L LINDSAY

M A, a woman aged 30, had a goiter removed eleven years ago and has had fainting spells since. Nine years ago she had a laparotomy. A physician told her that she is still having menopausal symptoms.

Pigmentation began six months ago on the malar region of the left cheek, and it spread to the right cheek and down the face. The urine was normal. The lesions consist of macular brown defined patches covering most of the forehead and a portion of the cheeks. The brown color of the lesions is evenly distributed.

**DISCUSSION**

DR M E OBERMAYER There is a history of oophorectomy, the patient menstruates scantily. Endocrine therapy may perhaps influence the chloasma.

DR ANKER K. JENSEN In the Year Book of Dermatology and Syphilology for 1936 there is a summary of an article by Dr Ferdinand Hoff in which he states his belief that abnormal skin pigmentations are due to a deficiency of vitamin C. In the Year Book of Dermatology and Syphilology for 1937, there is an article by Dr Theodore Cornbleet in which he also called attention to the role vitamin C plays in pigmentation. It is on the basis of these two articles that I have given ascorbic acid to patients who have chloasma. In a number of my patients I felt that there had been a decided improvement with a high intake of ascorbic acid. I suggest that this patient be given such treatment.

**Erythema Annulare Centrifugum** Presented by DR KENNETH L. STOUT

C. B., a man aged 51, has always enjoyed good health. One year ago he was complaining of a "bunch of ringworms." The original lesions developed on the left thigh, later spreading to the other thigh. Lesions on the left forearm appeared two days ago. The eruption comes and goes, unaffected by treatment and recurring in the same areas. The onset was eighteen months ago. I have observed him six times since his first visit. Individual lesions begin at a point, enlarge peripherally, heal in the center and after a longer or shorter period, usually several weeks, they clear up completely. Infrequent mild pruritus is experienced.

The general appearance is that of a well developed and well nourished middle-aged man in excellent health. When the patient was first examined, lesions were distributed over both thighs, on the inner and anterior aspects, and on the left forearm. There are seven lesions now, 3 are on the left thigh, 2 on the right thigh and 2 on the left forearm. They are annular, arciform and serpiginous, having a pink smooth elevated palpable margin which encloses a less elevated pigmented, slightly crinkled and scaly surface. Lesions vary in size from 2 to 10 cm in diameter.

Scrapings of skin from lesions exhibit no mycelium or spores. Phenolphthalein was given in a trial dosage, but it did not excite new lesions.

DISCUSSION

DR ROBERT WAKEFIELD When one sees eruptions like this, it is difficult to decide whether they are persistent erythemas or arc erythema multiforme. I have seen several patients recently who showed lesions with gyrate and annular figures clearing in the centers. Two gave histories of asthma and infantile eczema. One suspects an allergic background in this type of case.

DR KENNETH L. STOUT This is the type of case in which one keeps wondering what the cause is. I have never found anything. I considered the cause in the cases I have observed. In the last year I have seen four such eruptions. Every one of them was considered ringworm and treated as such, by either the patient or the referring physician.

**Ulcerative Late Syphilis of the Throat (Good Results from Treatment with Penicillin)** Presented by DR PAUL D. FOSTER

R. W. P., a white man aged 39, had a chancre five years ago, located 2 inches (5 cm) to the right of the base of the penis in the region over the right external inguinal ring. Six weeks later secondary lesions developed. Several months after the original infection he noted a small area of soreness in his throat which ultimately ulcerated, and the ulcer enlarged to about 2.5 cm in diameter. He has received continuous weekly

antisyphilitic therapy for the past five years. He also had eight treatments of fever therapy before April 1944. In April 1944, the serologic reaction of the blood was still strongly positive.

An irregular-healing indurated ulcerated area involved almost the entire left posterior portion of the pharynx, the left tonsillar and buccal areas and the soft palate. There is a scar 2.5 cm above the base of the penis. The blood pressure is 158 systolic and 90 diastolic. There is some hoarseness. Two months ago the Wassermann reaction of the spinal fluid was negative. The colloidal gold curve was normal.

A biopsy specimen from the throat on microscopic examination showed no evidence of a histologically specific type of inflammation. There was no evidence of malignancy.

Beginning on May 16, 1944, the patient received penicillin, 100,000 units daily for ten days, in a dosage of 20,000 units every three hours given intravenously.

DISCUSSION

DR SAMUEL AYRES I believe that this sort of case of therapeutically resistant syphilis is extremely rare. I have never encountered one, but if the history given is correct and the patient has received antisyphilitic therapy at a reputable clinic the effect of penicillin in this case seems rather striking. I think that it is worthy of report. I should also like to ask whether any one who has been checking up on the results of penicillin in the treatment of syphilis has seen any effect of the drug on neurosyphilis.

DR MOLLEURUS COUPERUS A similar case was reported at Mayo Clinic six months ago with a late syphiloderma, treated with penicillin, which also cleared up in a short time.

DR PAUL D. FOSTER This is the first patient with syphilis I have treated with penicillin. In view of the fact that he had had six years of antisyphilitic therapy and four separate courses of hyperpyrexia with no apparent permanent benefit, this case is a rather striking example of the almost miraculous effects of this new therapy. I gave him 100,000 units a day for ten days. At the end of three weeks all the ulceration had disappeared, and the patient complained of a dry throat as a result of the permanent scar tissue resulting from the cure of the gummatous lesion.

**Pseudopelade** Presented by DR A. FLETCHER HAMILTON

W. A. S., a white man aged 42, first noticed loss of hair in a nickel-sized patch on the left temple one year ago. Some regrowth of the hair took place. Since then numerous small areas with loss of hair have appeared on the top of the scalp without any regrowth. He is the proprietor of a woman's apparel store. His general health is excellent. The top of the head shows numerous separate and confluent small round and oval areas with complete loss of hair. These areas vary from 3 to 15 mm in diameter, but the majority are smaller than 10 mm in diameter. The skin of the involved areas is pinker than that of the uninvolved part of the scalp. Only an occasional dilated follicular orifice is present. Although no definite evidence of atrophy is visible, each hairless area seems palpably hollowed out in a saucer-like depression. No "exclamation point" hairs are present, and there is no lanugo undergrowth or other evidence of regrowth. The appearance of the involved portion of the scalp has remained unchanged since it was first examined, two months ago.

4 **Case for Diagnosis (Ulerythema Acneiforme?)**  
Presented by DR KENNETH L STOUT and DR M  
E OBERMAYER

W F, a white man aged 53, was first examined  
De year ago. He was complaining of bald areas  
involving the scalp and the beard. Each lesion began  
a slightly raised red eruption, progressively spread-  
g away from the center and having an active border,  
om which pus could be expressed. The central  
areas became hairless, smooth and flesh colored. The  
onst lesion developed fifteen months previous to the  
tient's first visit. It was on the left side of the scalp,  
ollowed within six or eight months by lesions on the  
ght cheek, and two or three months later a lesion  
curred on the left cheek. The patient had been under  
e care of a dermatologist for two and a half months  
1937 for "ingrown hairs" on the right side of the  
ck. This area healed after ten roentgen ray treat-  
ents had been given.

The man is well nourished, and his general physical  
amination revealed normal conditions, except for cu-  
aneous lesions. The scalp in general appears clean and  
vered with gray hair, except for four areas of alo-  
cia, varying from 1 to 3 cm in diameter. An oval  
ea 3 cm in diameter is in the left parietal-occipital  
gion. It is smooth, white, atrophic and slightly de-  
pressed. A few hairs are present, and a few pitted  
ars and scattered giant comedos are present near  
e margins. The border is slightly elevated, and pus  
n be expressed from some points. Over the right  
rietal area there is a chain of three bald lesions, the  
rgest being 3 cm in diameter. The margins of these  
eas are inactive and noninflammatory. Both cheeks  
e involved with irregular areas of alopecia, each  
aving a depressed atrophic surface and a slightly pig-  
mented margin. One lesion is raised and red on the  
ght side of the neck, and this lesion, the patient states,  
oks like the other lesions of the cheek when they  
gan. A lesion on the right cheek measures 3.8 by  
2 cm, below this, at the base of the neck, there is  
ircular area 3.8 cm in diameter. On the left cheek  
ere is an area 1.5 by 1.2 cm.

The urine was normal. There were a normal number  
erythrocytes, and the amount of hemoglobin was  
ormal. The result of the tuberculin patch test was  
gative.

The patient had typhoid in 1912, bursitis of the left  
oulder in 1928, extraction of all his teeth in 1928, a  
nsillectomy in 1930 and a period of nervous exhaustion  
r two or three years beginning in 1935.

Biopsy showed epithelial cystlike formations filled  
th degenerate epithelial cells, extending down from  
e epidermis into deeper parts of the cutis. Much  
und cell infiltration surrounded these structures.

Six injections of bismuth subsalicylate in oil had no  
fect on the eruption. Twelve intravenous injections  
gold sodium thiosulfate seemed to have no significant  
fect, although the patient thought that fewer pustules  
curred on the left side of the scalp, which has been  
e only one showing activity while under observation.

#### DISCUSSION OF THE TWO PRECEDING CASES

DR PAUL D FOSLER The first case is rather typical  
pseudopelade. There are no papules or erythema,  
id as far as I could see there was no atrophy. I am  
ot sure about the diagnosis in the second case. It  
ems to me that the atrophy of the areas of the scalp  
id face suggests lupus erythematosus. The patient  
ated that these erythematous lesions disappeared about  
month ago, after he had received gold therapy.

DR CLEMENT E COUNTER The first case is typical  
pseudopelade, with no pustular lesions nor other evidence  
of inflammation. I favor the diagnosis of folliculitis  
decalvans for the second case.

DR H C L LINDSAY Lupus erythematosus, favus  
and pseudopelade which have been treated lose part of  
their clinical characteristics, therefore, a student ex-  
amining the areas of atrophic alopecia should be warned  
that treated patients may have lesions that look some-  
what similar to one another and that a history aside  
from a biopsy study may determine the diagnosis.

DR KENNETH L STOUT I think that the first case  
is one of pseudopelade. The second, puzzled me  
when I first saw it, about one and a half years ago.  
I was at a loss to classify it. The first diagnosis that  
occurred to me was lupoid syphilis. An interesting fea-  
ture is the occurrence of scarring alopecia on both the  
beard areas and the scalp. The lesions of the scalp  
had a few pustules near their margins. Giant comedos  
were more conspicuous when I first saw the case. The  
lesions in the area of the beard did not have any  
activity during the period of observation. The lesions  
on the right side of the scalp appeared inactive when  
first seen, but now they have pustules. The lesions did  
not respond to bismuth or gold therapy.

DR M E OBERMAYER I believe that the eruption  
in the second case corresponds to an entity described  
by Unna, Rille and Gans termed "ulerythema acne-  
forme." This is characterized by the formation of flat  
erythematous papular plaques, which spread peripherally.  
After reaching a certain size, the erythema fades and  
comedo formation and atrophy set in. Eventually a  
uniformly atrophic scar is left. The section presented  
conforms with the microscopic picture described by  
Gans, namely, hyperkeratosis of the epidermis and the  
hair follicles, moderate but defined acanthosis with be-  
ginning atrophy as evidenced by the disappearance of  
the rete pegs, large comedo-like keratotic plugs, a  
multilobular cellular infiltrate which consists mainly of  
lymphocytes, some edema and rarefaction of the upper  
part of the dermis. I am glad that several members  
remarked on the resemblance of this disease to lupus  
erythematosus. The similarity in location and in the  
slow peripheral spread of the lesions is suggestive. We  
have studied and treated the patient from this point of  
view. So far, the disease has not responded to gold  
therapy. Inoculation of a guinea pig with excised tissue  
from one of the lesions did not produce pathologic  
changes visible at autopsy. That the disease seems to  
represent an entity of its own is brought out by differ-  
ential diagnosis. In pseudopelade clinical signs of in-  
flammation are absent, folliculitis decalvans lacks the  
characteristic comedo formation, folliculitis keloidalis is  
characterized by keloidal scars. We believe that we  
are dealing with a rare entity, the etiologic features of  
which are yet unknown. It is interesting that the  
histologic picture of the disease is not unlike that en-  
countered in the acneiform dermatosis produced by  
chlorinated hydrocarbons.

**Multiple Sarcoids (Boeck)** Presented by DR A  
FLETCHER HALL

In D C, a white woman aged 36, the first lesion  
occurred two years ago, just above and posterior to  
the left iliac crest. It was pink at the onset, and  
gradually it turned brown. Later similar lesions have  
appeared in the pubic area. Two lesions are on the  
scalp, and others are scattered on the trunk. The most  
recent lesions are on the upper lip. There are no sub-  
jective symptoms. No treatment has been applied.

There is no history of tuberculosis in the patient or in her family. She has had alopecia areata at intervals during the past three years.

Her general appearance is that of a woman in normal health. In the left flank there is a 1 by 2 cm regular well bordered oval plaque, which is smooth and slightly depressed. The center feels more compressible than the surrounding skin, and it is pale and atrophic, while the main portion of the plaque is a café-au-lait color. There is a patch on the right side of the back of the neck similar in every respect to the first, except that it is about half the size. The anterior aspect of the right labium majus shows a dime-sized round patch which is similar to the others but does not show as much pigment, the greater proportion of the center of this patch is pale and atrophic, and no hair is present. Similar but less well defined lesions appear on the left labium majus and on the left side of the scalp. The right half of the upper lip is the site of one large and one small split pea-sized lesion, both of which are slightly elevated and are pink rather than pigmented. There is the suggestion of a depressed center in the lower larger lesion.

Biopsy showed several small sharply defined masses of epithelioid cells and a few giant cells. Deeper in the cutis there were a few scattered giant cells. Few leukocytes were seen in the section. A later report of the roentgen ray examination of the chest described the presence of milary lesions throughout the lung parenchyma.

## DISCUSSION

DR PAUL D FOSTER I think that the lesions in the pubic area are suggestive of granuloma annulare. The lesions on the body and in other areas are not as typical, but they certainly could be a diffuse type of granuloma. The slide was compatible with the diagnosis of granuloma annulare, and that is my diagnosis.

DR SAMUEL AYRES I think that the color, consistency and distribution are all compatible with the diagnosis of sarcoid.

DR ROGERS WAKEFIELD I agree with the diagnosis of sarcoid. A new lesion on the right shoulder is more typical of sarcoid than are the older lesions.

#### Epidermolysis Bullosa Hereditaria Presented by DR ANKER K JENSEN

M L M, a white infant aged 13 months, had vesicular lesions soon after birth. These have occurred in crops ever since. The infant's father has had a similar eruption at intervals since his infancy.

Numerous vesicular lesions are present on the face and the extensor surfaces of the hands. Some are crusted, others show recent healing. A few lesions are healed in the center but still have a crusted border. There is slight atrophy of the skin in the site of healed lesions. The sites of some healed lesions are pigmented.

## DISCUSSION

DR SAMUEL AYRES This eruption does not seem to fit the typical picture of epidermolysis bullosa. It is widespread, even involving the mouth. In the case of the father there has been no loss of finger nails or toe nails, even though he has had the disease since infancy. The present eruption in the father is around the neck. This suggests a chronic benign familial pemphigus rather than epidermolysis bullosa.

DR ANKER K. JENSEN I believe that this is epidermolysis bullosa in which the lesions are sparse and

do not lead to atrophy or scarring. This patient presents characteristic bullae, and, from what the mother states, they often follow known traumas. I shall be glad to present the patient at a later date.

DR SAMUEL AYRES Why does the father not lose his finger nails and toe nails if he has had the disease all his life?

DR W H GOECKERMAN I think that one sees gradations of epidermolysis bullosa. The types differ materially. Like Dr Ayres, I am not sure that this is a case of true epidermolysis bullosa.

DR ANKER K JENSEN What procedure should follow to verify such a diagnosis?

DR M E OBERMAYER Biopsy and study of porphyrin metabolism might be of value.

#### A Case for Diagnosis (Pigmented Purpuric Lichenoid Dermatitis of Gougerot and Blum) Presented by DR CLEMENT E COUNTER

E B, a white woman aged 28, began to have a brown patchy eruption on the sides of the feet four years ago. The eruption has been macular throughout its course. Its onset was during the first summer she lived in Hartford, Conn. Before going to Hartford, she had always lived in Buffalo. Gradual extension of the eruption has taken place in the past two years. The present appearance is that of irregular brown macular lesions on the sides and tops of the feet and on the ankles, extending up the legs to a level of about 10 cm above the ankles. Individual lesions are 6 to 8 mm in diameter, irregular outline and often confluent. In places there are small slightly depressed atrophic lesions 2 to 4 mm in diameter and in other places dark red telangiectatic points or lines. There are no palpable varicose veins of the legs. A Kline test of the blood elicited a negative reaction. Biopsy showed dilated superficial veins, proliferation of connective tissue in the cutis. There was an infiltrate of both lymphocytes and leukocytes. Basal cells of the epidermis were pyknotic.

## DISCUSSION

DR WILLIAM MULVEHILL (by invitation) I believe that this is a case of Majocchi's disease because there is a lack of lichenification which is ordinarily seen in the Gougerot and Blum disease and because of the fact that on the histologic slide I observed in several places a considerable distention of the capillaries. This has not been seen in the lichenoid dermatosis suggested by Counter.

DR SAMUEL AYRES There is something about this case that is not entirely clear to me, because on clinical inspection the areas showing the present purpuric type of lesions are interspersed with many little scars. The patient states that she has not had any ulcers or pustules. However, there must have been something that caused those scars. It seems that there may have been a toxic eruption, possibly a tuberculid-like manifestation. I think that tuberculin tests would be in order.

DR H C L LINDSAY The largest scar was caused by trauma. The other scars are slight. In appearance the location of the involved area can be covered by half-length riding boots—i.e., the eruption extends over the vamp and halfway up the shin. The sharp conspicuous line of purpura terminates at a level with the top of such a boot. An area on the ankle of the right foot forms a perfect circle. Other indistinct circles are visible. The diagnosis of Majocchi's disease seems correct.

DR M E OBERMAYER I am inclined to call this eruption Majocchi's disease. Ultimate atrophy is present

the syndrome and therefore aids in confirming the diagnosis. It is certainly not a lichenoid dermatitis. DR CLEMENT E COUNTER I was unable to see any regular character to the distribution of lesions, otherwise the case would have been presented as one of lichen planus annularis telangiectodes. When it began, four years ago, it was restricted to the sides of the feet. Time of the lesions may be simple excoriations, because the patient also has insect bites.

**Acrochordosis Lipoidica Diabeticorum** Presented by DR SAMUEL AYRES JR

B, a white woman aged 21, has had lesions on her shins for two years. These lesions seemed to follow traumatic injuries. She has had diabetes for six years. The present treatment of her diabetes includes the daily use of 40 units of protamine insulin.

Her general appearance is that of a normal young woman. The lesions are limited to the shins and consist of irregular vertically oval areas. The lesion on the left shin is an oval area about 4 inches (10 cm) long. The right shin has two separate lesions. All lesions are brownish red with a translucent appearance. There is telangiectasia in places, and there also are numerous pinhead-sized whitish, almost milium-like, circular points. The surfaces are superficially atrophic.

#### DISCUSSION

DR WILLIAM MULVEHILL (by invitation) I agree with the diagnosis, but I should like to have Congo red injected into some of these lesions because they have the appearance of an amyloid disturbance. I think that this might be enlightening.

DR KENNETH L STOUT There may be localized amyloid degeneration, evidenced by the yellowish brown streaks.

DR M E OBERMAYER I cannot see how any one can arrive at a diagnosis without biopsy. The suggestion of amyloidosis is constructive.

DR SAMUEL AYRES JR As yet there has been no opportunity to perform a biopsy. I think that the reaction is characteristic. An unusual feature is the presence of milium-like bodies within the lesions. It is my impression that aside from attempts to control diabetes there is no valuable local therapy. There seems to have been a slight improvement by the local use of roentgen rays.

**Infectious Eczematoid Dermatitis (Resistant to Therapy)** Presented by DR CLEMENT E COUNTER

B, a man aged 58, began to have itching lesions over his body about six months ago. The scratching of these itching spots, known to him as "hives," produced excoriations in various places. The excoriations of the heel scar on the right leg failed to heal. About four months ago he accidentally stepped through a hole in the floor, further traumatizing his legs. At present, the legs are covered uniformly with a weeping crusted eruption. The margins are sharp at various places, such as near the knees and on the dorsa of the feet. There are round and oval scaling patches on the anterior parts of the thighs and on his back.

The Wassermann reaction of the blood was negative. The urine contained a moderate amount of albumin. The hemoglobin content was 15.8 Gm per hundred cubic centimeters. Erythrocytes, 5,870,000 and leukocytes, 900 of which 76 per cent were neutrophils, 23 per cent lymphocytes and 1 per cent monocytes.

Various treatments have been tried in the past three months including continuous application of wet dress-

ings of a solution containing approximately 0.25 per cent zinc sulfate and 0.12 per cent cupric sulfate (Albion water). Later foot baths of the same solution were administered. Soaks in potassium permanganate solution (1:8,000) were used. Oleovitamin A, 75,000 U S P units daily, has been given with riboflavin tablets. Six roentgen ray treatments, each 75 r, were given. A shake lotion was applied locally which contained 10 per cent each of talc and corn starch and 8 per cent glycerin in lime water. Powdered sulfanilamide and petrolatum dressings have just been used to the ankles. Intravenous injections of calcium gluconate were given three times a week. A lotion containing glycerite of tannic acid in hamamelis water has been used locally, as well as sulfanilamide and sulfadiazine in alcohol as a lotion.

#### DISCUSSION

DR PAUL D FOSTER It seems to me that baths in potassium permanganate solution (about 1:2,000 or 1:3,000) would help this man a great deal. In addition to this, supportive therapy, such as vitamins and diet, must be taken into consideration.

DR KENNETH L STOUT I suspect that an infection may be found in the urinary system, either the bladder or the prostate, which may be the sensitizing factor. Local treatment, of course, is a problem.

DR ROGERS WAKEFIELD In this type of case I think that it is worth while using the autohemoc therapy extensively. I was interested in the fact that the dermatitis on the right leg developed on an old scar. I could not see the scar well, but I think that it would be worth while for one to take a roentgenogram of that part of his anatomy to see whether there is any low grade infection in the periosteum or the bone.

DR ANKER K JENSEN As a therapeutic measure I suggest potassium permanganate baths and local application of 2 per cent solution of gentian violet medicinal followed by 5 per cent boric acid ointment.

DR SAMUEL AYRES JR This eruption represents an extensive staphylococcus infection on the legs with a secondary id reaction elsewhere. The patient apparently had hives and in scratching himself infected the old scar on his leg, and the infection gradually spread to involve the whole leg. Infections like this will not stand too vigorous treatment. I do not know whether he has had treatment with sulfathiazole ointment or not, but I should be somewhat afraid that it might have sensitized him. I would give him some wet packs of saturated solution of boric acid together with paintings with gentian violet medicinal, then apply 10 per cent boric acid ointment and continue with gentian violet medicinal.

DR M E OBERMAYER I am sure that the recommendations of Dr Ayres for local treatment are valid. Yet I should emphasize not the factor of infection but rather that of the high degree of sensitization which is undoubtedly present. Hence general desensitizing measures, such as autohemoc injections, therapy and daily generalized ultraviolet irradiations in slowly ascending doses, appear indicated.

DR W H GOECKERMAN Probably by chance, I have had the misfortune to see a good many of these cases within the last year. My first thought was that war conditions might be a factor, possibly the factor. Most of the patients had been treated elsewhere with no results, nor did I get any satisfactory response. The eruptions seemingly cleared up temporarily by one method of treatment or another and then would relapse in an acute manner. I looked on them as a diffuse

infectious eczematoid dermatitis and at first wondered whether an occupational factor might be responsible. However my patients belonged to all classes, and I could not find a common denominator to account for them. I am surprised that none of the other members have seen so many of them. I was rather impressed that these patients were nervously overtaxed and high-strung but this suspicion is vague, and blaming the disease on the nervous system may be putting the cart before the horse. The ordinary infectious eczematoid dermatitis as described by Engman, is, of course, rather common and if one can find the focus of infection is usually amenable to treatment. My results in these cases have not been satisfactory, and I doubt that Dr. Counter will have a good response. If he should be successful, I should like to hear from him at the next meeting.

DR STANLEY ANDERSON I should classify the disease as an infectious eczematoid dermatitis. I understand that it started on his legs as an infection superimposed on a vascular stasis.

DR WILLIAM MULVEHILL Dr Urbach believes that these patients have become sensitized to the products of their own cell destruction. No matter what is done for them, an id eruption develops over the body.

DR CLEMENT E. COUNTER The possibility of a stasis eczema was considered, and I used a fixed dressing with Unna's paste. The dressing had to be removed in less than one week because of increased discomfort. The process had extended under the fixed dressing. The potassium permanganate solution that has been used was of a 1:8,000 dilution. This man has had sulfathiazole powder on his ankles, with a plain petrolatum dressing to hold it there. Sulfathiazole crystals were identified in the urine four days after that treatment was instituted. The lesions have never exhibited thick purulent exudate.

DR W. H. GOECKERMAN I have tried the sulfonamide drugs, but they did no good.

DR SAMUEL AYRES Sulfonamide drugs have a tendency to sensitize such a patient.

DR H. C. L. LINDSAY Sulfathiazole ointment seems to cause more allergic reactions in my own patients than the sulfanilamide ointment.

NOTE—It was later reported that this patient improved promptly after three transfusions of whole blood (1 pint [470 cc.] each) and the intramuscular injections of extract of liver (2 U. S. P. injectable units to each cubic centimeter). Boric acid solution and 5 per cent boric acid ointment were the local applications. He left the hospital in one month and was entirely well in three months.

#### Lupus Erythematosus Presented by DR M. E. OBERMAYER

E. H., a white woman aged 43, had an erythematous eruption on the right ear six months ago, which slowly spread to the other ear, the neck and the back. The subjective sensation was mainly that of burning. Local therapy, which included roentgen ray treatment, was of no benefit. Five months ago an acute, edematous and erythematous eruption covered diffusely both ears and dusky erythematous maculopapules of the erythema multiforme type, varying from 0.5 cm. to several centimeters in diameter, were present on the nose, the neck and the upper part of the back. With application of bland medicaments the eruption gradually disappeared but left a considerable degree of hyperpigmentation especially on the neck. Six weeks after treatment was

begun, the only active inflammatory lesions were the small scaling erythematous macules on the right upper lid and near the left eye and an infiltrated plaque with indurated borders, 2 by 3 cm. in extent, in the center of the upper part of the back. Several weeks later recurrence of the eruption on the neck took place at the exact site of the former lesions, in the form of purplish erythema and fine scaling. Biopsy of such lesion on the neck was performed. The eruption subsided again slowly, and at this time the patient presented (1) hyperpigmentation on the site of former lesions on the neck, (2) the two small erythematous maculopapules on the face and the indurated plaque on the back, which were previously mentioned.

There were 3,600,000 erythrocytes and 115 Gm. hemoglobin. The leukocytes were normal in number and kinds. Roentgen ray examination of the teeth did not reveal focal infection.

Biopsy showed follicular plugging, liquefaction necrosis in the epidermis and a large amount of lymphocyte infiltrate in the corium.

#### DISCUSSION

DR MOLLEURUS COUPERUS The lesion on the back suggests erythema annulare. The lesion on the face was the one from which the specimen was removed for biopsy, and the microscopic picture is compatible with the diagnosis of lupus erythematosus.

DR W. H. GOECKERMAN It seems to me that it would be hard to make a diagnosis clinically at the present time.

DR M. E. OBERMAYER This case presents several interesting features: (1) the acute onset in the form of an erythematous and edematous dermatitis, suggesting a drug eruption from iodides with features of erythema multiforme, (2) the spontaneous remission and exacerbations occurring at fixed sites, which is likewise suggestive of a drug eruption, and (3) the combination of the superficial, hyperpigmented type of eruption with deep-seated lesions resembling granuloma annulare. I think that the histologic features of this section (follicular plugging, liquefaction necrosis and the massive infiltrate) leave little doubt as to the correctness of the diagnosis of lupus erythematosus. In the subacute form with a tendency to hyperpigmentation, a variety which does not have a good prognosis.

#### Tuberculosis Miliaris Faciei (Rosacea-like Tuberculosis of Lewandowsky) Presented by DR M. E. OBERMAYER

J. H., a white woman aged 32, has had an eruptive of eight or nine years' duration on her face. It has been recurrent. There is only slight itching.

The general appearance is that of a frail but healthy looking woman.

Two months ago the rosacea oval of the face showed erythema, telangiectasia and occasional pustules. In addition, there were closely set small maculopapules only a few millimeters in diameter, which were level with the surface and reddish brown. These were present on the chin and on the surrounding parts of the neck. These lesions left brownish-yellowish papules on direct pressure. One month of treatment directed against rosacea resulted in the disappearance of the rosacea syndrome but did not influence the brownish-yellow papules.

A general physical examination by an internist did not reveal pulmonary tuberculosis. The tuberculin test with 0.0002 mg. of purified protein derivative elicited



doubtful reaction, but the reaction was positive when 5 mg was used. Biopsy showed small collections of epithelioid cells in the upper part of the dermis, unrelated to the follicles, and a perivascular lymphocytic infiltrate.

# DISCUSSION

DR WILLIAM MULVEHILL (by invitation) I, too, looked closely for the lesions. When the patient called attention to them, one could see them. On looking at the section, I think that the diagnosis is correct. There are circumscribed areas of epithelial cells which are incompatible with the Lewandowsky tuberculid.

DR STANLEY ANDERSON I should like to ask whether the syndrome cleared up before the patient had the injections of the gold salt.

DR M E OBERMAYER Yes. Treatment for rosacea was given for the first few weeks, and only after the primary lesions of rosacea had disappeared was gold therapy begun. I presented this case for two reasons, first, to illustrate the not infrequent combined occurrence of rosacea and tuberculosis miliaris faciei and, second, to show the relative inconspicuousness of the lesions in Lewandowsky's disease. Both features account for their being unrecognized frequently.

**Lymphoblastoma** Presented by DR M E OBERMAYER

E W, a white man aged 40, fifteen years ago noticed lesions beginning to appear on the scalp, which were characterized by their chronicity and lack of subjective symptoms. They did not differ essentially from the lesions which are present at this time. Periods of involution alternated with periods of recurrences, but his scalp never cleared completely. In March 1942 a lesion similar to the ones on the scalp appeared on the left temple. He has diabetes, which is now controlled. The patient was thoroughly studied at the Vanderbilt Clinic, New York, in 1933-1934. These examinations, as well as later periodic check-ups, did not reveal pathologic changes other than those of the skin.

The patient is a healthy-looking, well nourished man, who has a macular lesion with a central scar from a previous removal of tissue for biopsy on the left temple. The lesion on the scalp has enlarged and is now indurated. Ten months ago an indurated and slightly elevated plaque with a small livid surface, 2.5 by 2.5 cm in extent, was present on his left temple. A well defined livid macular area, several centimeters in diameter, was present on the right anterior aspect of the scalp. A biopsy specimen from the plaque was taken and the slide presented. After this procedure the eruption underwent partial spontaneous involution but recurred several months later in its former size. Within six months of treatment, the plaque slowly disappeared. No differential counts of the blood (in January and May 1944) showed no essential changes from the normal. Biopsy showed a massive infiltrate in all parts of the dermis, composed mainly of mononuclear cells which had large hyperchromatic nuclei and only a small amount of cytoplasm. A few cells contained mitotic figures. There were also some larger cells with vesicular pale nuclei. No Sternberg-Reed cells could be identified. Nine intravenous injections of colloidal sulfur have been given, and 6 intramuscular injections of ethyl sulmoograte also have been administered.

# DISCUSSION

DR MOLLEURUS COUPERUS The man who saw this patient first, fifteen years ago, was Dr Oppenheim, in

Vienna. He had then lesions similar to those he has today. Dr Oppenheim told him to forget about them. The clinical appearance of the lesions suggests lymphoblastoma. I was unable to see the tissue section. Probably the original lesions were not the same as those seen today.

DR SAMUEL AYRES I thought that the lesions clinically suggested lymphoblastoma, and yet the long duration would be against it. I am wondering whether there is a possibility of a type of sarcoma. I also wonder whether the patient's diabetes could cause a toxic cutaneous manifestation to look like this. The patient will bear further watching.

DR W H GOECKERMAN The clinical picture would favor lymphoblastoma, but I do not know how to fit that in with the history of all these years' duration. It is an extraordinary case if one can eventually prove that the eruption is a lymphoblastoma.

DR M E OBERMAYER This case is interesting because of the long duration and the evidently benign course of the disease, as I was informed by Dr George C Andrews that the case was extensively studied in 1934 at the Vanderbilt Clinic. At that time, several elevated and firmly indurated plaques of a red color were present over the left parietal area of the scalp, while macular brownish scaly lesions involved the skin beneath both axillae, the chest, the neck and the inguinal areas. Roentgen ray examination of the skull showed essentially normal conditions. Microscopic sections showed many features suggesting mycosis fungoides and others suggesting Hodgkin's disease. Several years later the patient was seen by a physician in Los Angeles. At that time, not only the microscopic section but also the blood picture suggested leukemia of the lymphocytic type. The prompt involution of the lesions following roentgen ray therapy was considered another indication of the correctness of the diagnosis. From the recent section presented today, I consider the disease a lymphoblastoma of the leukemic or pseudoleukemic type rather than true mycosis fungoides. Whether or not the patient's diabetes is a factor in his cutaneous eruption remains doubtful.

## PHILADELPHIA DERMATOLOGICAL SOCIETY

CARMEN C THOMAS, M D, *Chairman*

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Sept 15, 1944

**A Case for Diagnosis** Presented by DR CARMEN C THOMAS and DR MARGARET J GERLACH (by invitation)

J R, a white woman aged 59, somewhat overweight, presents atrophic, slightly brownish mottling on the neck and on the extensor surfaces of the forearms. On the anterior aspect of the abdomen and on the back are scattered circinate and patchy infiltrated lesions, dusky red in color. On the dorsa of the hands there are annular lesions with infiltrated margins. In March 1944 maculopapular brown-red lichenoid lesions developed on the dorsa of the forearms. Some were annular with depressed centers. The eruption spread to the neck and the upper part of the chest. Early in July 1944, dusky red plaques developed on the abdominal wall and the back. These have become larger. The earlier lichenoid lesions disappeared, leaving slight atrophy.

Biopsies of the plaques were performed on March 27 and April 24, and a histologic diagnosis of chronic non-specific granuloma was made on the basis of focal accumulations of leukocytes with occasional Langhans giant cells. There was no evidence of fat deposits in frozen sections. The serologic reactions of the blood for syphilis were negative. A roentgenogram of the chest was normal.

The patient has been given thirteen weekly intramuscular injections of 0.2 Gm of bismuth subsalicylate and local applications of 2 per cent ichthammol in paste of zinc oxide.

## DISCUSSION

DR CARROLL S WRIGHT: The lesions on the hands resemble those of lichen planus undergoing involution. They exhibit central umbilication, and several are annular. I suspect that the eruption on the abdomen had nothing to do with that on the hands. The patient has an inflamed patch on the abdomen, and I questioned her to learn whether she had applied any plasters. She said that she had not, but the eruption looks like a local irritation producing urticaria-like lesions.

DR HERMAN BEERMAN: I think the histologic structure is as near that of tuberculosis as one can expect, at least there is a definite chronic granuloma.

#### Raynaud's Disease, Syphilis of the Central Nervous System

Presented by DR HERMAN BEERMAN and DR HENRY MORGAN (by invitation)

P W T, a white man aged 43, thin and poorly nourished, with a long history of peripheral vascular disturbance, presents a grayish, circumscribed, oval ulceration about 6.3 cm in diameter, with a grayish base and irregular edges on the right ankle, associated with generalized edema of the dorsa of both feet. This was preceded by a generalized patchy superficial scaly pyogenic eruption in March 1944. It was associated with a gangrenous ulcer on the right ankle. The eruption cleared up quickly. The patient had a penile lesion in 1921 and an indefinite history of secondary syphilis at that time. There is a history of chronic alcoholism. A sympathectomy for Raynaud's disease was performed in 1939. The serologic tests of the blood for syphilis gave positive reactions in 1939, the patient received eight injections of a bismuth preparation and irregular treatment with arsphenamine. Serologic tests in recent years have yielded negative reactions.

The Kolmer reaction of the blood on Feb 24, 1944, was anticomplementary, the reactions to the Eagle and the Kline precipitation tests were negative. On June 20, the serologic tests resulted as follows: Kolmer Wassermann, anticomplementary, Eagle, negative, Kline precipitation, weakly positive, and Kline, negative. On July 11, 1944 these results were observed: Kolmer, 32 units, Eagle, doubtful, and Kline, positive (2 plus). On Aug 9, 1944, examination of the cerebrospinal fluid revealed: cells, 0, protein, 50 mg per hundred cubic centimeters, Wassermann reaction, 1244, and colloidal gold curve, 1222210000. An examination of the cerebrospinal fluid on September 6 revealed the presence of red blood cells, a total protein content of 40 mg per hundred cubic centimeters, a Wassermann reaction that was positive (0112) and a colloidal gold curve of 2221110000.

The leukocyte count on June 23 was 6,850.

A roentgenogram of the right ankle on June 27 showed slight irregularity of the periosteum over the internal malleolus. The changes were minimal, there was no evidence of any involvement of the underlying bone.

#### Morphea-Like Scleroderma

Presented by DR HERMAN BEERMAN and DR HENRY MORGAN (by invitation)

C H, a white man aged 31, pale, emaciated, partially crippled and very weak, presents an erythematous scaly, nonelastic skin, which feels hard and immobile and is cracked and painful to the touch. There is atrophy of the muscles of the legs, ankles and feet with complete loss of function of these parts. There are scattered pigmented plaques. The patient operates a knitting machine. He uses no tobacco, drinks beer occasionally and takes no drugs. He enjoyed excellent health until about three years ago, when, after "rheumatic fever," small, blister-like lesions developed on the feet and ankles. These blisters would break and form crusts. They were accompanied with pain and burning. Later there was considerable itching, followed by boardlike hardening and immobility of the affected parts, which resulted in loss of function of the feet and amputation of the right toe. The disease progressed and a few months later involved the hands and arms resulting in complete immobility and contracture of both hands (claw hands). Patchy pigmentation and whitish elevated oval plaques are present on the chest.

The patient has false teeth. His blood pressure 120 systolic and 80 diastolic. His pulse rate is 100 and his respiration rate 22. His heart is not enlarged and there are no cardiac murmurs. The liver and spleen are not palpable. Genitourinary examination is noncontributory. The pronounced muscular atrophy makes it impossible to elicit reflexes, sensation is impaired for the same reason. The cranial nerves are normal.

A roentgenogram of the chest on Sept 8, 1944 shows normal conditions. A roentgenogram of the knees and ankles on Sept 7, 1944 revealed demineralization of bones of the knees and ankles, the joint spaces well preserved. The only abnormality noted was certain degree of demineralization, such as is frequently associated with a diminished blood supply. Determinations of blood chemistry on September 6 showed: urea nitrogen 13 mg, sugar 110 mg and uric acid 64 mg per hundred cubic centimeters. A urinalysis on September 6 gave normal results, except for the presence of leukocytes. The Kolmer and Kahn reactions of blood were negative.

## DISCUSSION

DR HERMAN BEERMAN: The values for calcium and for phosphorus were normal. Is it usual for scleroderma to develop into a morphea-like type on the body after the appearance of diffuse lesions?

DR JOHN H STOKES: That can occur. It can start with the sclerodermatous type on the fingers and develop into a morphea-like type, but it is unusual for scleroderma to start with sclerodactylia and produce stiffening of the tissues of the face followed by diffuse development. I do not know whether the keloid characteristics of the lesions of the chest were noticed; they were not at all like those of morphea or scleroderma.

DR CARROLL S WRIGHT: How much can be expected from neostigmine?

DR CARMEN C THOMAS: In our series of 20 cases, the results have been good. The dose has to be pushed to 8 or 9 tablets daily, 75 mg every three hours. When this is continued over three or four months, there is considerable softening of the infiltration.

DR JOHN H STOKES: I thought that I had previously brought to the attention of the society the obs-



ions of two or three French dermatologists on the effect of bismuth in the treatment of multiple and isolated lupoid-phic lesions, in which Major Flood and I have been interested. I think that bismuth has done more for multiple morphea than any other form of treatment I have seen used. The preparation first employed was a French preparation of bismuth hydroxide, which was not curable in this country before the collapse of France. Shortly after the French description of the response to bismuth, another observer obtained results with an iodine bismuth compound, so we gave 1 of our patients iodobismutol with benzocaine (Squibb) and 2 an American-made suspension of bismuth hydroxide. As far as we could see, the results with bismuth hydroxide were somewhat better than those with iodobismutol, but some of the reasons for this was that the patients were more readily discouraged with iodobismutol because of the irritability of the local reactions when injections were not properly given. We do not begin to see results until after about ten to fifteen weeks of bismuth therapy. Then the involution in 2 of our cases was really beyond belief. I have not seen such results in other dermatous processes before. The patients were young women. Another patient improves if she takes bismuth with sufficient intensity, but the process begins to recede when she slackens up during a rest period. I prescribed mecholyl bromide in rather large doses in addition to the bismuth, and since then she has been cured. She has, however, had to stop taking mecholyl because of vomiting. The bismuth therapy certainly is not infallible, but I have already begun to receive a number of inquiries from physicians who have seen some of the patients who have been treated at a distance, saying that the results are remarkable and wanting to know the details of the technic. I commend it as something to try. A course of fifteen weeks with two injections a week of iodobismutol is given, one injection of bismuth hydroxide must be given before the process begins to undergo involution. Then another course of fifteen weeks, or perhaps altogether three courses of twelve weeks, is about as far as I have gone. In 1 case of lichen sclerosus with bandlike morphea across the chest, the result was exceptional. The patient improved so that she lost the sense of stricture, the band of morphea became soft and faded, and the lichen sclerosus disappeared completely.

**DR J V KLAUDER** In the early days of bismuth therapy of syphilis, I used bismuth hydroxide, which I prepared by suspending it in olive oil. The mixture was sterilized and injected intramuscularly.

**DR JOHN H STOKES** This is an oil suspension.

**BERCULOSIS CUTIS, Lupus Vulgaris, Inactive Osseous Tuberculosis** Presented by **DR CARMEN C THOMAS** and **DR MARGARET J GERLACH** (by invitation).

**DR R.** A white man aged 44, well nourished but unable to walk without the aid of canes, presents on the right cheek a scarred, atrophic lesion, in the neighborhood of which there are many nodules which are intensely red on pressure with a diascop. Similar translucent nodules appear on the helix and lobe of the ear. The patient's family history is negative for tuberculosis and other illnesses. At the age of 16 the patient was hospitalized for two years with tuberculosis of the spine. At that time a reddish, pea-sized nodule developed on the right cheek and enlarged slowly during the years. At first the patient was completely paralyzed but after three years was able to walk with aid of a brace. Roentgenograms of the chest at no

time have shown evidence of pulmonary involvement. Later tuberculosis of the bone developed in the left arm, and in 1939 the left hip became involved. In 1941 a right orchiectomy was performed for tuberculosis. The facial lesions continued to spread slowly, with development of new nodules and partial healing in other sites. On the basis of a biopsy on May 15, 1944 of a specimen from the upper part of the left ear a diagnosis of tuberculosis cutis was made. There was no evidence of caseation in the section. The Kolmer, Kline and Eagle reactions of the blood were negative for syphilis.

Treatment in the past has been carried out in many hospitals and clinics with roentgen rays and radium, which produced a slight aggravation. Parts of the lesion have at times been destroyed by surgical excision, trichloroacetic acid, curettage and electrodesiccation. Ultraviolet irradiation has also been employed. Lately, the nodular borders have been treated with solid carbon dioxide, resulting in complete flattening of the lesions and excellent cosmetic results.

#### DISCUSSION

**DR J V KLAUDER** I saw the patient a number of years ago, when his lupus was active and his appearance in striking contrast to what it is now. He has made out extremely well.

**A Case for Diagnosis (Exfoliative Dermatitis, Premycotic Mycosis Fungoides?)** Presented by **DR STEPHEN WHELAN** (by invitation).

**B P.** A white woman aged 56, presents a blotchy red skin with generalized weeping and scaling. A few small red nodules have appeared in the past few weeks. There is cervical, axillary and inguinal lymphadenopathy. The present illness had its onset a year ago after her ninth injection of an arsenical, when general exfoliation occurred. There was an exacerbation three weeks ago, although no more bismuth or arsenic was given in the past year. A positive reaction of the blood for syphilis was found in 1943, and she was given thirty-two injections of a bismuth compound.

A complete blood count resulted in normal values. A urinalysis revealed 5 to 7 leukocytes per high power field, the urine did not contain bismuth, arsenic or porphyrins. A culture of the blood produced non-hemolytic *Staphylococcus aureus*. Examination of the cerebrospinal fluid showed nothing abnormal. The Kolmer, Kline and Eagle reactions of the blood for syphilis were positive. The glucose tolerance test showed fasting, 76 mg per hundred cubic centimeters, at one-half hour, 128 mg, and at one hour, 134 mg.

The report on the biopsy specimen was as follows: exfoliative dermatitis (?), premycosis fungoides (?), parakeratosis, edema and acanthosis, somewhat polymorphic infiltration.

#### DISCUSSION

**DR BERNARD L KAHN** This is a typical case of exfoliative dermatitis following arsenphenamine. Four patients were sent to our service at a hospital by a physician whose practice it was to administer 9 decigrams of arsenphenamine per dose. They had practically the same symptoms as described in this case, fainting after the first injection and appearance of exfoliative dermatitis about a month later.

**DR JOHN H STOKES** I might remark that she was given penicillin in accordance with a concept of exfoliative dermatitis which is a little different from the usual arsenical drug eruption concept. My colleagues and I regard the arsenicals simply as the sensi-

tizing trigger mechanism in a good many of these cases, not as causes of true arsenical dermatitis but as activators of hemolytic pyogenic infection to which the patient is allergic or rendered allergic by the use of arsenicals. This is somewhat like the Milian biotropism concept. Accordingly, this woman is being treated with penicillin for a hemolytic staphylococcus dermatitis. My inclination is to classify exfoliative dermatitis following use of an arsenical drug as a sensitization dermatitis-infection phenomenon.

DR BERNARD L. KAHN: Would not exfoliative dermatitis develop in any person who was given a big dose of arsphenamine, irrespective of how sensitive he may be to the drug?

DR JOHN H. STOKES: I should not say so, that has not been my experience. The size of the dose and the number of doses may have something to do with it, but they are not the prime movers in the situation. But just one dose would rarely produce a dermatitis. When the enormous number of injections and the extremely high dosage in common use are considered, it is not primarily a function of dose, I should say.

DR HERMAN BEERMAN: It should be mentioned that Schoch (Schoch, A. G. *J. A. M. A.* 98:1367 [April 16] 1932) produced exfoliative dermatitis in a sensitive patient with the washings of arsenic left in the syringe and needle. In spite of its having been washed thoroughly, the traces of arsenic in that syringe were sufficient to cause an exacerbation of exfoliative dermatitis in a previously sensitized person.

COMMANDER H. E. TWining (MC), U. S. N. R.: What dosage of penicillin do you employ, and how long is it used?

DR JOHN H. STOKES: The dosage of penicillin in staphylococcal infections of the skin is undecided because we have not been able to get enough. However, we have decided arbitrarily that we must use 200,000 to 400,000 units for four, five or seven days to get an effect. That results in notable improvement. For 1 patient with hemolytic staphylococcus infection with extensive lesions in the mouth almost suggesting early pemphigus, 1,200,000 units improved the eruption a great deal. Another 1,200,000 units together with sulfathiazole transformed the clinical picture. The patient now is 75 to 85 per cent better.

COMMANDER H. E. TWining (MC), U. S. N. R.: How long do you continue the dosage if you get no results?

DR JOHN H. STOKES: I would give up to 1,200,000 units if the patient did not improve with 200,000 to 400,000 units. Sometimes one sees a patient become worse instead of better, in which case it is probable that he is allergic to impurities in the penicillin.

COMMANDER H. E. TWining (MC), U. S. N. R.: The commonest reaction that we have seen is urticaria. We have had only 2 cases in which we have had to discontinue the drug in a series of 200.

DR JOHN H. STOKES: With hemolytic staphylococcal infections, I think that one is dealing with highly allergic persons and should expect more trouble with them. In the nonallergic person, urticaria is the reaction. In an article by Welsh and Rostenberg in a recent issue of *The Journal of the American Medical Association*, there is an interesting study of sensitivity to tuberculin produced by penicillin. From that article one gets the impression that in a number of persons penicillin can produce a tuberculin type of reaction. Of course, the workers with penicillin are subject to allergy

all the time, but it is assumed that it is the process or the impurities, not the penicillin.

#### A Case for Diagnosis (Multiple Hemorrhagic Sarcoma of Kaposi, Granuloma Pyogenicum) Presented by DR ANTHONY SABETTA (by invitation) and DR CARMEN C. THOMAS

T. H., a white man aged 48, presents on the inside of the left foot, 3 cm. below the malleolus, 1 growths of different sizes. The larger is hemispherical, 2 cm. in diameter, smooth surfaced, easily bleeding, attached to the base by a small pedicle. The smaller one is 1.5 cm. in diameter and has the same characteristics. Both have a mushroom-like appearance. Together with these two growths there is another which has an angiomatous appearance, on the plantar region of the left foot. In the popliteal region and the dorsum of the right hand there are flat angiomatous lesions. All lesions have become painful lately. On the inner side of the left foot four months ago a small tumor appeared, which has persisted to date, growing continuously. At the same time, on the plantar aspect of the same foot there appeared a nodular lesion in the popliteal region and on the dorsal surface of the left hand some red lesions. Histologic examination of a biopsy specimen from the left ankle suggests pyogenic granuloma (hemangioma?). One from the third finger on the left hand showed no abnormality.

#### DISCUSSION

DR J. M. SCHILDKRAUT, Trenton, N. J.: I think that this is a case of Kaposi's sarcoma. It has been my experience that when some of these lesions become pedunculated and granulomatous and bleed easily, assists to remove them. One of my patients had them on the skin, in the gums and on the tonsils. The lesions in the mouth responded to roentgen therapy. The ordinary Kaposi lesions also responded to roentgenotherapy.

DR CARMEN C. THOMAS: Would you destroy lesions with electrosurgery or roentgen rays?

DR J. M. SCHILDKRAUT, Trenton, N. J.: I used to destroy them on the skin with electrosurgery, and they healed beautifully. Those in the mouth I destroyed with roentgen rays.

DR CARROLL S. WRIGHT: I think that the lesions could be removed fairly readily from the foot. They would probably heal, but of course he would get more pain. However, he would be much more comfortable for a while.

#### *Erythrose pigmentaire péribuccale* (Brocq)? Erythema Rhinophyma, Tinea Vesicolor. Presented by DR JOHN W. LENTZ

H. W., a white woman aged 35, moderately obese, with slightly prominent eyeballs, slightly enlarged thyroid and moderate edema of the ankles, presents (1) brown hyperpigmentation of the center of the face, more prominent on the chin, with the exception of the area around the lips, which seems to be normal, (2) slightly bulbous nose with enlarged pores, and a yellow-brown patchy cutaneous eruption scattered irregularly over the thorax and cubital fossae. The appearance of the tongue is suggestive of avitaminosis. The patient has had fronto-occipital headaches for past fifteen years. She has had hypertension for seven years, with a blood pressure of 248 systolic and 170 diastolic. After exertion dyspnea and edema of the ankles develop. She also complains of nocturnal palpitation and nocturia. She has lost 20 pounds (9.1 Kg.) in the last two years. Many years ago

suffered from menstrual syncope and recently from menorrhoea. She is presented for diagnosis of a chronic cutaneous eruption of some ten years' duration, considerably aggravated by exposure to sunlight. There is occasional accentuation of the eruption during menstruation, with only a slight burning discomfort. There is no history of ingestion of drugs. She has had no recent treatment. During an exacerbation, the patient's face assumes a brilliant red hue. Her nose has become more prominent during the past few years, with enlargement of the pores. A brown-yellow, patchy eruption on the nose, axillae and cubital fossae has been present for an indefinite number of years, with exacerbations. The patient's father, mother and one sister died of hyperactive cardiovascular disease.

Dr. S. blood count revealed essentially normal findings. Serum blood urea nitrogen level was 13 mg per hundred centimeters, the fasting blood sugar 89 mg and urea clearance 92 per cent. A urinalysis gave normal results.

# DISCUSSION

Dr. J. M. SCHILDKRAUT, Trenton, N. J. It is my impression that this is a case of seborrheic dermatitis. The patient has much dandruff and a greasy erythematous eruption on the face, there are prominent follicular lesions on the nose and a suggestion of oily seborrhea.

Dr. MORRIS MARKOWITZ. I think that the periorificial infiltration is consistent with the diagnosis offered.

Dr. BERTRAM SHAFFER. That does not account for the lesions in the cubital spaces or around the thorax. They do not look like parapsoriasis.

Dr. CARROLL S. WRIGHT. The diagnosis of tinea versicolor could be confirmed or ruled out in two minutes. I would prefer the diagnosis suggested by Dr. Schildkraut, namely, that the whole process is seborrheic. I think this case really ought to be re-discussed at the next meeting with reference to what the scrapings showed and whether the facial eruption responds to a simple treatment for seborrhea.

Dr. MORE. The scrapings were subsequently reported as negative for tinea versicolor.

**A Case for Diagnosis (Herpes Simplex, Recurrent, Acne Varioliformis?)** Presented by Dr. EDWARD F. CORSON

C, a well nourished white man, aged 40, presents red scars scattered on the distal third of the nose. Among these, there are similar lesions but of a pinkish color, evidently appertaining to the most recent outbreak. A few less noticeable pits appear on the forehead. A folliculitis of the beard of two weeks' duration is also present. The patient's family history is noncontributory, and he recollects no illness of his own of any importance. For the past three or four years he has had occasional outbreaks on the end of his nose. These have occurred as a rule during the spring and fall months, when inflammatory vesicles appear, followed in due course by drying and crusting. The last attack occurred ten days ago and is now subsiding. The patient was recently discharged from the army after serving fourteen months.

# DISCUSSION

Dr. FRITZ CALLOWAN (by invitation). Because of the seasonal occurrence observed in this case and the location on the part of the face most exposed to sunlight, one is reminded of Hutchinson's "recurrent summer eruption" (hydroa vacciniforme), although these eruptions have been observed most frequently in younger subjects. Acne varioliformis produces small scars similar

to those on the nose of this patient. However, it has an extremely chronic course, independent of any seasonal factor. Herpes facialis when developed on the tip of the nose usually produces a more painful eruption accompanied with neuralgiform pain or soreness of the regional glands.

Dr. CARROLL S. WRIGHT. If it were herpes simplex, I do not think it would leave the type of scar he presents. I should like to see a 20 per cent sulfathiazole suspension rubbed into that area. I think it would clear up. I have treated a patient in that way, and he is now well.

**A Case for Diagnosis (Avitaminosis, Pityriasis Rubra Pilaris?)** Presented by Dr. CARROLL S. WRIGHT

R. S., a white boy aged 13 years, presents many discrete pinhead-sized follicular papules scattered over the trunk. These are grouped into patches anterior to each axilla. The eruption began about June 1, 1942 as follicular elevations. It is worse each summer. There are no subjective symptoms. The patient has had 300 units of roentgen rays applied to some of the areas.

# DISCUSSION

Dr. ALLEN D. KING, Wilmington, Del. I did not see enough lesions tonight of the pityriasis rubra pilaris type. I think that avitaminosis may be the diagnosis.

Dr. CARMEN C. THOMAS. That is not impossible, even though the diet is adequate. Peck and his co-workers (ARCH. DERMAT. & SYPH. 43:223 [Feb] 1940) postulated that pityriasis rubra pilaris is a metabolic disturbance involving the utilization of vitamin A, and therefore even in the presence of an adequate diet the disease may develop if there is some fault in the liver or elsewhere which prevents proper assimilation of vitamin A.

Dr. CARROLL S. WRIGHT. I favor giving vitamin A by injection. We had 1 patient, a boy, who had a severe eruption similar to this. When we gave him vitamin A by injection, it cleared up. He went into the army, and in six months it recurred. He was given vitamin A by mouth for three months without benefit and was sent home. We cured him again by injections of vitamin A.

Dr. FRANCIS B. EVELAND, Wilkes-Barre, Pa. I thought that some of the lesions looked like lichen nitidus but lacked the complete picture. There were no lesions on the shaft of the penis.

**A Case for Diagnosis (Fungous Disease, Lupus Erythematosus?)** Presented by Commander H. E. TWining (MC), U. S. N. R.

A. L., a white man aged 27, presents a sharply demarcated patch of dermatitis extending across the back and neck. It is slightly scaly in the center. The borders are inflammatory and in many areas are covered with thin crusts which when removed expose underlying eroded surfaces. The scales in the center of the patch are adherent, with a suggestion of atrophy. The eruption began four summers ago with itching and burning across the shoulders. It entirely disappears each winter and returns with the advent of hot weather. This is a new patient, and no treatment has as yet been instituted. Two brothers have similar lesions.

# DISCUSSION

Dr. LOUIS GOLDSTEIN. I think that this is the familial benign chronic pemphigus described a few years

ago by Hailey and Hailey. In this particular case the lesions are vesiculosquamous. They occur on the neck, where trauma is a factor, the lesions are recurrent, and there is also a history of a similar eruption in some other members of the family.

DR CARROLL S WRIGHT: The two brothers and the cousin of this patient are patients of mine. They do not have exactly the same kind of eruption. They have it around the neck, but they definitely do not have pemphigus. All of them responded to the simplest treatment—about 50 units of roentgen rays and the application of solution of boric acid, ichthammol and solution of aluminum acetate. They have it in the summer and only around the neck.

DR MORRIS MARKOWITZ: The French have another name for it—recurrent impetigo.

DR CARROLL S WRIGHT: I regard it as some low grade infection, without being able to give it a name.

COMMANDER H E TWining (MC), USNR: I can say only that I have just seen this man. The thing that impressed me was that it might be lupus erythematosus or a fungous disease. I have sent scrapings to the laboratory for culture but have not yet had any report. An interesting sidelight is that all the men of the family except the father seem to have this disease. The mother and father are free, and so are the sisters. All the brothers, however, and one cousin have it, with the history of recurrence every summer for the last four summers. If it is of fungous origin, why does it recur every summer? It is certainly not *tinea versicolor*.

DR REUBEN FRIEDMAN: I have a clergyman under my care with a similar picture involving the neck and upper region of the back. He has had annually recurrent attacks in the late spring or summer, clinically identical with that shown tonight. I think that the eruption is due to decreased local resistance together with trauma and hyperhidrosis. What then occurs is a moniliasis attended by a secondary low grade staphylococcic or streptococcic infection. I have been able to clear up the eruption with the application of Castellani's paint. It dries the oozing discharge, and the crusts eventually fall off. Involution occurs in a short time.

DR BERNARD L KAHN: I have had similar cases, my best results have come from administration of a suspension of microform sulfathiazole, which clears up the dermatitis nicely. It is seen only around the neck, where the perspiration is especially irritating in summer.

## CLEVELAND DERMATOLOGICAL SOCIETY

BENJAMIN LEVINE, M D, *President*

GEORGE W BINKLEY, M D, *Secretary*

Sept 28, 1944

**Acanthosis Nigricans, Benign Type with Acne and Active Duodenal Ulcer** Presented by DR G W BINKLEY and DR JAMES H BARR

R G, a Jew aged 29, was previously presented before the Cleveland Dermatological Society with a diagnosis of acanthosis nigricans (ARCH DERMAT & SYPH 34 704 [Oct] 1936). He is presented again by the department of dermatology and syphilology of University Hospitals, Cleveland, with the added history that the eruption of the skin has been present since the age

of 2 weeks. During 1941, he was treated with ultraviolet irradiation, vitamins and a tonsillectomy. Bellevue Hospital in New York city.

There is a generalized eruption, which is more severe on the right side. The reaction involves the vertex of the scalp to the right of the midline, right axilla more than the left and so on for the involvement down to the feet. There is partial alopecia of the scalp. A hyperkeratosis of the palms and soles is symmetric.

The chief lesion is an ill defined, verrucous plaque with papillomatous masses projecting almost 1 cm on the right axilla, in the groin and on the penis. Other lesions are flat, poorly defined, hyperpigmented macules or plaques. In thick plaques, the natural skin cleavage lines are deepened. The central portions of the plaques have a dirty appearance, while the edges have the usual brown hyperpigmentation. Comedones, scars and a few acne papules are present on the forehead, sternal area, upper part of the back, abdomen, thighs. There is purulent discharge from the right ear.

The urine on examination was normal. The hemogram revealed erythrocytes 4,690,000, a hemoglobin content of 86 per cent (Sahli) and leukocytes 6, with a differential of 59 per cent polymorphonuclear leukocytes, 27 per cent lymphocytes, 3 per cent large monocytes, 9 per cent eosinophils and 2 per cent basophils. The Kline reaction of the blood was negative. Examination showed no occult blood in the stool. The basal metabolic rate was minus 14 per cent. Sedimentation rate was 0.65 mm per minute. A roentgenogram of the chest showed no abnormalities. Roentgenograms of the gastrointestinal tract showed normal anatomy in 1936. On March 10, 1944 a fluoroscopic roentgenographic examination of the gastrointestinal tract showed hypertrophic gastritis and duodenal ulcer with niche formation. A biopsy of the skin showed squamous cell papilloma, with some increased pigmentation in the corium.

Therapy with 150,000 U S P units of vitamin B<sub>12</sub> given intramuscularly for eight days resulted in visible improvement of the cutaneous lesions.

## DISCUSSION

DR JOHN GAMMEL: There is no clinical or laboratory evidence of mycosis in this case. I understand that cultures have been made of material from erythematous lesions, which were probably crusts of organisms. Material should be taken by aspiration of fluid from fresh lesions. Organisms may be slow in growth. Therefore, the culture tubes should be observed for a minimum of two weeks.

DR G W BINKLEY: This man is shown again to bring out certain points which were not apparent and not stressed in 1936. There is the statement that cutaneous reaction is of congenital origin. This history places the acanthosis nigricans in the benign group. Dr Helen O Curth (ARCH DERMAT & SYPH 353 [Sept] 1936) reported on a 15 year old Jew youth with the benign type of acanthosis nigricans and severe acne. In our case there are large comedones present both in the usual areas of seborrheic acne and in the skin of the abdomen and anterior aspect of thighs. This suggests that acne in these cases may be a symptom of the disease.

There is no evidence to indicate that the gastric and duodenal ulcer are a mucous membrane manifestation of acanthosis nigricans. This possibility may be considered, since Ormsby and Montgomery (Diseases of the Skin, sixth edition, Philadelphia, Lea

unger, 1943, p 528) have stated that small discrete verrucous and warty growths have been observed on other parts of the mucous membranes, including the epiglottis and pharynx.

# **Required Generalized Anhidrosis with Localized Hyperhidrosis Presented by DR JAMES H STRAUCH**

V M, a white man aged 35, presented from the Department of dermatology and syphilology of University Hospitals, Cleveland, was a physical education instructor in perfect health. He entered the Army in 1942 and about six months later noticed profuse sweating of the hands, feet and face. This was always related to overheating from exertion or environmental temperature. He had several episodes diagnosed as heat exhaustion, with weakness, headaches, dizziness and nausea. Participation in sports or exposure to the hot sun resulted in profuse abnormal sweating of the face, hands and feet as well as symptoms of headache, dizziness, palpitation, nausea and weakness. However, no rash appeared on any other part of the body at these times.

In the past history reveals no serious illnesses, and the systemic review shows normal conditions. He has no change of hair or changes in the nails. There is no family history of a similar condition or of hereditary defects. Examination (at room temperature, 32 C) reveals a well-built, muscular man with normal pubic hair, axillary and facial hair. There is profuse sweating of the face, neck, hands and feet. There is a slight amount of perspiration in the axilla and inguinal regions. All other areas are exceptionally dry and smooth. The skin over the trunk and arms shows few hairs, and there is a mottled pigmentation of the skin. There is a patchy type of alopecia of the scalp, with atrophy of the areas of alopecia. The toe nails show extensive Newborn discoloration. There are a few vesicles in the lines of the palms. The teeth are normal. The examination shows some prognathism. Examination of the heart, lungs, abdomen, reflexes and sensory nerves shows normal conditions.

Various results of the urinalysis and the hemogram were normal. The blood urea nitrogen level was 16.5 mg per hundred cubic centimeters. A glucose tolerance test revealed a fasting blood sugar level of 68 mg per hundred cubic centimeters, at the end of one-half hour 110 mg per hundred cubic centimeters, and at the end of one hour 85 mg per hundred cubic centimeters. Blood clearance was 55 per cent of normal the first time and 75 per cent of normal the second time. Examination of the spinal fluid showed Pandy and Ross-Reddy reactions negative and a cell count of 3 lymphocytes and 2 polymorphonuclear leukocytes. The protein was 46.8 mg per hundred cubic centimeters, and the 1944 index was 719 mg per hundred cubic centimeters. Biopsy 123 milliequivalents, the colloidal mastic curve was normal, and the Wassermann reaction of the spinal fluid was negative. The basal metabolic rate was 66 per cent. Cutaneous biopsy showed a few leukocytes around the smaller vessels and a few normal hair follicles and sebaceous glands. Sweat gland ducts were relatively few, they were slightly dilated and lined with cuboidal and low columnar cells. The sweat gland ducts were slightly reduced in number in all sections. A roentgenogram of the vertebrae showed no deforming spondylosis of the lumbar vertebrae. The size of the bones was within normal limits. A roentgenogram of the sella turcica showed overbridging of the sella and an increase in the thickness of the table of the skull.

The patient was placed in an electric blanket. The rectal temperature rose to 39.8 C (103.6 F) in one and one-half hours. At the end of that time, the skin of the trunk was dry, but there was profuse sweating of the head, neck, hands and feet but only slight sweating in the groin and axilla. He complained of dizziness and nausea. A starch-iodine test was performed, and a blue reaction confirmed the fact that sweating occurred only in the areas of sensible perspiration (figure). Mecholyl bromide 10 mg, produced no sweating on the trunk or extremities.

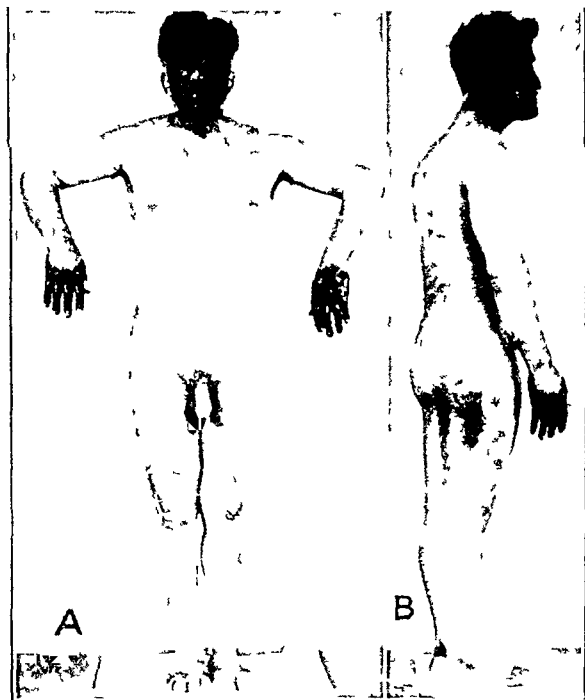


Fig 1—A, anhidrosis of the trunk with hyperhidrosis of the head, hands and feet, B, generalized anhidrosis with localized hyperhidrosis

## DISCUSSION

DR HAROLD N COLE We should not pass lightly over the work done on this patient by Dr Strauch. The remarkable thing was the making of a diagnosis. I saw this patient and did not have the slightest idea what he had. It is interesting how the areas of perspiration and anhidrosis have been defined on this patient.

DR BENJAMIN LEVINE There is a new drug called hexanol which stimulates perspiration. I shall be glad to supply it to any of those present who would wish to experiment with it. It is a 6 carbon unsaturated aliphatic alcohol.

CAPT HENRY C ROBERTELLI (by invitation) I have studied 8 patients selected from 77 that were suffering from various types of injury due to heat. All 8 patients recovered within two months. The patient presented would probably have been put in the same group, however, his condition has persisted for eighteen months in spite of treatment.

## **Acrosclerosis with Raynaud's Disease Presented By DR HAROLD N COLE and DR JAMES H BARR**

L K, a white woman aged 40, entered the hospital with a chief complaint of thickened and discolored skin of approximately two years' duration. The patient had been in good health until four years ago, at which time

signs and symptoms of Raynaud's disease developed, involving both hands and the third and fourth toes of the left foot. About two years later, she observed that the skin of the chest was becoming thickened, mottled brown and white and pruritic and was covered with fine scales. Within a month or so, her fingers became involved similarly, with limitation of motion. Ulcers of the ends of the fingers healed with a stellate scar. Within the past year and a half, the process has become more generalized, involving the remainder of the trunk, arms, neck and face, with progressive loss of hair over the involved areas. The patient does not remember the order of the progression. The nails were brittle and broke readily. There is a past history of cholecystitis, recurrent renal lithiasis and spastic colon. There is no family history of a similar ailment.

The skin of the face is taut, the nose is narrowed, and there is some slight decrease in the size of the mouth. The skin of the trunk is thickened, smooth, mottled brown and white and bound down to underlying tissue and yet is moderately pliable. The neck, arms, hands and trunk and a small patch 3 by 4 cm on the medial aspect of the right foot are all similarly involved. There is limitation of motion in the afflicted areas of the extremities, but especially of the hands.

The basal metabolic rate, urine and hemogram were normal. Gastrointestinal study showed absence of peristalsis, obliteration of mucosal markings and slight dilatation of the esophagus. The duodenum and stomach were normal. Roentgenograms of the hands showed normal bones. A roentgenogram of the chest showed an increase in pulmonary markings in the lower portion of the right lung. Microscopic examination of the skin of the trunk showed changes consistent with scleroderma.

Pruritus seemed to have been aggravated by neostigmine methylsulfate, 0.25 mg three times a day, given subcutaneously. However, after two days of this therapy, she felt that limitation of motion, especially of the face, had become less. Clinically the skin seemed more pliable. At present, she is taking neostigmine bromide, 0.015 three times a day by mouth.

#### DISCUSSION

DR HAROLD N COLE: This patient's difficulty started in the tips of her fingers, as is the case in acrosclerosis. In the beginning, she had symptoms which were consistent with Raynaud's disease. Only later did the process develop on her face and trunk. This case belongs in the group of cases of acrosclerosis of Seller.

DR JAMES H BARR: Her skin is not typically board like but rather pliable. She has esophageal changes consistent with acrosclerosis and subjective symptoms resultant therefrom. There is slight dysphagia, especially noticeable while the patient is drinking in the semirecumbent position.

**A Case for Diagnosis (Sarcoidosis? Granuloma Annulare?)** Presented by DR EARL W NETHERTON and DR W R HUBLER

Mrs S B, a white woman aged 45, is presented from the Cleveland Clinic. She noticed a single, raised, ringlike lesion on the back of her neck six months ago. Since then many similar persistent lesions have appeared on the neck, face and arms. The eruption has been somewhat pruritic at times. Various soothing and stimulating ointments have been used by the patient, with no improvement. For a mild arthritis, she has taken vitamin D capsules for one and one-half years.

There is a reddish brown eruption, consisting of discrete and confluent infiltrated lesions confined chiefly to the extensor surfaces of the arms, the entire neck and the upper sternal region. A few less well defined lesions are present on the forehead, shoulders, flexor surfaces of the forearms, dorsa of the hands and upper part of the trunk. The individual lesions are on an average about 0.5 cm in diameter and have raised, rolled reddish brown peripheries and flat, slightly depressed centers. On the arms and sides of the neck the ringed lesions have partially fused. On the back of the neck, the ringed areas have flattened entirely, leaving an area of brownish pigmentation half the size of a palm, partially surrounded by a rolled red border. Some of the older lesions show slight diffuse scaling.

The hemogram and values for blood sugar were within normal limits. The Wassermann and Kahn reactions of the blood were negative. A roentgenographic examination of the chest revealed normal conditions. A tuberculin test (1:100 dilution old tuberculin) elicited a negative reaction.

Histologic examination of a portion of a representative lesion revealed no epidermal changes. There were numerous large nodules occupying most of the dermis. These areas showed disruption of the connective tissue, scattered lymphocytic infiltration and numerous well defined nests of cells composed of epithelioid cells with vacuolated cytoplasm and a few pyknotic nuclei. Numerous giant cells with peripherally placed nuclei were found. The blood vessels in the papillary and superficial layers were dilated. There was thickening of the intima of an occasional small vessel.

Treatment has consisted of a total of twelve weeks of doses of 75 r of low voltage roentgen therapy to the neck and a somewhat smaller number of doses to the other involved areas. There has been some involution of the lesions, particularly those on the back of the neck, following this treatment.

#### DISCUSSION

DR HUGO HECHT: There is a symmetric involvement. I think that the disease is a lichen planus in an unusual form. It seems too extensive for granuloma annulare.

DR EUGENE STERN: The patient had a hysterectomy about four years ago and has not menstruated since. This could be a case of photosensitivity.

DR ROY L KILE (by invitation): In this case, one should examine an isolated lesion. One of these looks like granuloma annulare. The anatomic changes resemble those of sarcoid, but clinically the picture is more like granuloma annulare.

DR HAROLD N COLE: I never saw Boeck's disease with so many lesions. They are also the wrong color for that disease. I hesitated to make a diagnosis of sarcoid because the histologic picture was not definitely that. I wonder whether this could be erythema elevatum diutinum.

DR EARL W NETHERTON: Lichen planus was considered, but the lesions were lemon colored and Wickham's striae were not present. The striking thing was the uniform size of the lesions except where they were together. It is certain that they are granulomatous lesions of some kind. We lean toward the diagnosis of an exaggerated type of granuloma annulare.

DR W R HUBLER: Because of the possibility of granuloma annulare, low voltage roentgen therapy was given. However, the lesions have not responded well to roentgen irradiation. The problem is further therapy.



Harry Goldblatt, pathologist, gave a histologic report of a chronic granulomatous inflammation of tubercular type.

DR BENJAMIN P PERSKY The widespread clinical distribution and the ring form suggest granuloma annulare. Histologically, a basophilic granular degeneration of the connective tissue of the dermis is consistent with granuloma annulare. Further features of granuloma annulare were the scattered epithelial cells and the perivascular infiltrate. In places this infiltrate was dense enough to suggest a beginning tubercle formation. The involvement of blood vessels and the absence of definite parasites was against sarcoidosis. Therefore, the histologic evidence is stronger for granuloma annulare.

# Case for Diagnosis (Periarteritis Nodosa?)

Presented by DR JAMES H BARR

B, a white man of 60, presented from the department of dermatology and syphilology of University Hospitals, Cleveland, has had recurring purpuric lesions involving the entire body but especially the trunk and limbs at remissions. Lesions are annular and discrete, with a well defined, raised, indurated, erythematous border and a central clear area. Distribution is diffuse and symmetric. The lesions are extremely pruritic and tend to appear spontaneously, leaving an area of permanent brown pigmentation. The patient has also had unexplained fever, leukocytosis, eosinophilia, moderate albuminuria, impaired renal function, cerebral vascular disease, generalized lymphadenopathy, optic neuritis, hepatomegaly, splenomegaly and anemia. There is, in his past history, a past history of two similar episodes, one, a year and a half years ago, and one, one month before the present admission, at which time the diagnosis of erythema multiforme was made. Biopsies of muscle and lymph nodes at that time failed to show anything significant. The lesions tend to come in crops, remitting spontaneously in two to three weeks. The patient became asymptomatic free on one occasion, during an episode of pneumonia accompanied with high temperature.

The first biopsy revealed a thickened epithelium with elongated keratinocytes projecting into the underlying tissue. The basement membranes were intact. There was a moderately severe perivascular infiltration with eosinophilic leukocytes and large mononuclears throughout the dermis. There were numerous extravasated red blood cells. The sedimentation rate was 1 mm per hour. The urine showed a specific gravity of 1.010, albumin (2 plus) and occasional white blood cells in sediment. The hemogram revealed a leukocyte count of 6,000 and 2,620,000 erythrocytes, with a hemoglobin content of 52 per cent. The differential count showed 60 per cent polymorphonuclear leukocytes, 19 per cent lymphocytes, 3 per cent large monocytes, 16 per cent eosinophils and 1 per cent basophils. The urea nitrogen was 20 per cent of normal.

## DISCUSSION

DR EARL W NETHERTON This is a striking case because of the fever, the eosinophilia and the fact that the lesions come and go. I thought of periarteritis nodosa.

DR HAROLD N COLE This patient has been under observation for years. He has severe pruritus and elevated temperature and is seriously ill. All kinds of remedies have been made. Cultures of the blood were sterile. The patient reminded me of a patient observed at Cleveland City Hospital with a diagnosis of periarteritis nodosa. This patient does not have areas of

necrosis. Periarteritis nodosa is the diagnosis proposed in this case, even though there is no evidence to support it in the muscle biopsy.

CAPT HENRY C ROBERTELLI, MC, AUS (by invitation) Was there any involvement of joints or extreme pain? Usually there are swelling of the joints, pain and edema in such cases.

DR JAMES H STRAUCH He has had pains in the joints in the past but no edema.

## Metastatic Melanoblastoma Presented by DR JAMES H STRAUCH

G R, a white man aged 76, is presented by the department of dermatology and syphilology of University Hospitals, Cleveland. He entered the hospital with flaccid paralysis of both legs of one month's duration.

A severe generalized arteriosclerosis, associated with mental deterioration, is found. There is a flaccid paralysis of both legs, paralysis of the bladder due to injury of the cord and loss of rectal sphincter tone. There is moderate inguinal adenopathy and moderate, irregular, hard, nodular enlargement of the prostate. The liver and spleen are not palpable. Many well defined, discrete, freely movable hard blue nodules are found in the dermis of the trunk and extremities. They are not attached to the overlying skin and are not tender. They vary from 0.5 to 2 cm in diameter. Ophthalmoscopic examination shows no intraocular tumor.

The hemogram showed a moderate anemia. Urinalysis revealed a heavy trace of albumin and a positive benzidine reaction. The Kline exclusion reaction of the blood was negative. Examination of the cerebrospinal fluid revealed a xanthochromic fluid containing fresh red blood cells. The initial pressure was greatly decreased. The Pandy reaction was strongly positive. The total proteins were 863 mg per hundred cubic centimeters. The chlorides were 631 mg per hundred cubic centimeters. The colloidal mastic curve was 334542100. The Wassermann reaction of the spinal fluid was negative. The fluid jelled immediately in the tube. Biopsy of a subcutaneous nodule revealed melanoblastoma.

## DISCUSSION

DR JAMES H STRAUCH I have been unable to find the primary site of the melanoblastoma in this patient.

DR JAMES H BARR The paralysis and the change in the spinal fluid indicate involvement of the spinal cord by metastatic tumor. This involvement is undoubtedly diffuse and not localized to one level.

## Epidermolysis Bullosa Presented by DR JAMES H STRAUCH

J F, a white girl aged 11, presented from the department of dermatology and syphilology of University Hospitals, Cleveland, has had recurrent bullae on the feet and occasionally on the hands since the age of 6 weeks. The lesions occur with the trauma of ordinary walking, are painful and rupture with difficulty. They are more readily produced and more frequent in the summertime. Occasionally, the feet are so painful that she is unable to walk. There are no disturbances of hair, nails, eyes or other ectodermal tissues.

The family history reveals that the first known carrier of this defect migrated from Germany and that for seven generations his descendants had similar lesions. There was no intermarriage. There were thirty-seven close relatives affected, including the patient's mother. These persons were almost equally distributed between

the two sexes. If a person is born free of these lesions, none of his descendants have them—in one branch for five generations. In all cases, the lesions are worse in summer than in winter. Bullae do not disappear with increasing age. The patient's grandfather had bullae up to his death, at the age of 80. One aunt is able to suppress the appearance of bullae by working in a cold air-conditioned candy factory.

Examination reveals numerous clear bullae on the soles, varying from 1 to 4 cm in diameter. There are none on the palms.

## DISCUSSION

DR HUGO HECHT. This case is remarkable in that it is most unusual to trace a family history of similar disease back so far.

DR JAMES H. STRAUCH. The complete history showing that the defect was present in seven generations of the family indicates that the disturbance is a hereditary dominant.

## METROPOLITAN DERMATOLOGICAL SOCIETY

ROYAL M. MONTGOMERY, M.D., *President*

JAMES LOWRY MILLER, M.D., *Secretary*

Oct 16, 1944

**A Case for Diagnosis (Contact Dermatitis, Dermatitis Medicamentosa?)** Presented by DR LESLIE P. BARKER

The patient was first seen on Sept 28, 1944, at which time she gave a history of having had an attack of acute infectious conjunctivitis three or four months previously. She used "drops" in her eyes that produced an inflammation of the eyelids. Shortly afterward a few red, itchy macules developed on the neck, and since that time others have developed in the groin and on the thigh. She had taken no drugs internally but had used plant sprays as well as nail polish.

On her first visit she had one silver dollar-sized patch and one small (dime-sized) patch of erythema on each side of the neck near the shoulder that was slightly raised, scaling and crusted. Since that time, she has had smaller but similar lesions in the groin.

## DISCUSSION

DR J. LOWRY MILLER. Dermatitis medicamentosa is the most logical diagnosis. I should favor contact dermatitis if no history of ingestion of drug can be obtained.

DR THOMAS N. GRAHAM. I agree with Dr. Miller, but apparently, according to the history, contacts have been ruled out in this case. I believe that the eruption may be seborrheic dermatitis. The patient has considerable scaling of the scalp, typical of seborrhea. One often sees seborrheic dermatitis which is resistant to treatment, and I think that this diagnosis should be considered.

DR MAURICE J. COSTELLO. I agree with Dr. Graham. I think that this patient has a resistant type of seborrheic dermatitis. The locations which are affected are fairly common ones, the scalp, sides of the neck and groins.

DR ROYAL M. MONTGOMERY. I believe this to be a contact dermatitis. I think that patch tests with nickel sulfate and potassium bichromate should be performed.

Metal beads may contain either nickel or chromium. My second diagnosis is a drug eruption from phenolphthalein. She denies having taken this drug, but may have taken it unwittingly in pink cakes or candy.

DR LESLIE P. BARKER. I have treated the patient about ten times and have eliminated all sources of drug including the possibility of colored candy containing phenolphthalein. The lesions on the thighs have appeared within the last two weeks. At first they were bright red, edematous and oozing, although the acute phase has subsided.

NOTE.—In spite of discontinuation of the use of nail polish, sprays and eye drops and the use of roentgen ray treatments locally as well as soothing applications and injections of vitamin B complex, the eruption continued to progress and new lesions have developed. She is taking no drugs at all and has had several colic irrigations.

**Pityriasis Rosea Associated with Oral Lesions in a Child** Presented by MAURICE J. COSTELLO, M.D.

R. H., a boy 6 years of age, from Lenox Hill Hospital, outpatient department, has had a typical eruption of pityriasis rosea with the herald patch on the right shoulder for the past three days. This eruption is accompanied with match head to pea sized superficial, edematous lesions on the palate, the buccal mucosae, the tongue and the floor of the mouth. His temperature is 101.2 F by rectum.

## DISCUSSION

DR J. LOWRY MILLER. The boy definitely has pityriasis rosea, and the oral lesions are of particular interest to me, as I often looked for them but never have found them before.

DR THOMAS N. GRAHAM. It is the first case of pityriasis rosea in which I have seen oral lesions.

DR LESLIE P. BARKER. I think that this case is exceptionally interesting because of the oral lesions, the elevation of temperature. Some dermatologists think that lesions are present in the mouth in about 25 percent of cases of pityriasis rosea. This has certainly been my experience. Prodromal symptoms of headache, fever and general malaise are frequently seen in patients with pityriasis rosea.

DR ROYAL M. MONTGOMERY. This case is unusual, first, because the disease occurs in a young child, second because of the oral lesions.

DR MAURICE J. COSTELLO. I have seen oral lesions in children with pityriasis rosea more frequently than one would think, especially if the eruption is accompanied with fever. My attention was drawn to it by Quequierre of Philadelphia. He made the point that it was seen more in children than in adults. I have demonstrated them on several occasions in children. I have never seen them in adults.

**Purpura Simplex** Presented by DR J. LOWRY MILLER

S. H., aged 31, a single woman, complained of recurring attacks of petechiae for the past year. Lesions began about the ankles, but they have gradually extended to include the entire thighs. Her general health has been good. She has had no arthritic pains. She denies that she has taken any medicine by mouth for the past year.

Examination shows many pinhead-sized purpuric lesions which do not fade on pressure and, on the thighs particularly, some pea-sized to dime-sized sim-



On the legs, there are a number of brownish pigmented areas, the remains of previous active lesions. The mucous membranes are clear.

# DISCUSSION

DR THOMAS N GRAHAM Eruptions of this type are usually due to drugs or to foci of infection. There is no history of drugs in this case. The patient's tonsils are badly infected, and I believe that this infection may be the cause of the purpura. I think that she should have a blood platelet count, studies of bleeding and clotting time and a determination of the blood level of vitamin C in order to rule out a more serious hematosis.

DR RICHARD J KELLY I agree with Dr Graham. The patient has definite foci of infection which should be cleared.

DR ROYAL M MONTGOMERY The patient gave a history of swelling of the knees and ankles at various times when she had the eruption. I believe that the disorder is rheumatic purpura.

DR J LOWRY MILLER I think that one is justified in asking the patient to have her tonsils removed, as a number of patients respond to the removal of foci of infection.

## Case for Diagnosis (Lupus Erythematosus, Papulonecrotic Tuberculid?) Presented by DR J LOWRY MILLER

A 33 year old Negro woman, presented herself at the Vanderbilt Clinic today with lesions located on the face, ear lobes and arms, particularly the elbows. She stated that the lesions had occurred in crops on her arms for the past five years. The lesions last about three months and spontaneously clear, leaving white, thinning spots. They have recurred on the average every six months. Three weeks ago she noted lesions on the face for the first time. Her general health has been good except for a chronic vaginal discharge and recently pain in the left lower abdominal quadrant. She has been married for eight years, with no pregnancies. Blood tests for syphilis said to have elicited negative reactions. On the extensor surfaces of the elbow there are raised lesions of split pea-sized papules with pigmented, depressed centers. On the arms there are a few scattered, pea-sized erythematous papules. On the face there are a dozen pea-sized pigmented papules surrounded by erythematous rings. On the right cheek there is a pea-sized pigmented macule surrounded by erythema. On the left ear lobe, there are two pea-sized pigmented lesions which show slight atrophy. No laboratory reports available.

# DISCUSSION

DR MAURICE J COSTELLO If I had to make one diagnosis I should say that the patient probably has a drug eruption. I base it on the history. She has been taking B C Headache Powders (which contain salicylic acid, potassium bromide and acetylsalicylic acid) since the onset of menstruation. These lesions are surrounded by erythematous halos. The lesion on the left cheek appears to be a fixed eruption due to the action of some drug.

DR THOMAS N GRAHAM I think that this patient has erythema multiforme. She presents characteristic type of lesions on the face and on the extensor surfaces of the forearms. Although this type of lesion is most frequently observed on the dorsa of the hands, it is often seen in the areas of this patient's eruption.

Erythema multiforme is of course frequently caused by medication, and I think that in this case a drug is the most probable cause.

DR ROYAL M MONTGOMERY I think this eruption is caused by the ingestion of drugs. It may be called either a drug eruption or erythema multiforme from drugs. A specimen for biopsy should be taken from one of the lesions on the elbow and cheek to rule out lupus erythematosus and papulonecrotic tuberculid.

DR J LOWRY MILLER The patient came to the clinic for the first time this afternoon. About six dermatologists saw her under a good light, and all made the probable diagnosis of lupus erythematosus and papulonecrotic tuberculid. The lesions on her ear in good daylight appear atrophic.

NOTE—Microscopic examination of a biopsy specimen from a cutaneous lesion of the leg disclosed localized hyperkeratosis, a widening of the granular layer and infiltration of lymphocytes. A decided lymphocytic infiltration and aggregation of chromatophores was noted in the proximity of a hair follicle. The lesion was definitely papular and suggested lichen planus. However, there were deep, scattered, focal areas of infiltration, hence the possibility of lupus erythematosus must be considered as well as some type of lichen-planus like dermatitis medicamentosa.

After examining the patient clinically and reevaluating the histologic changes, I am of the opinion that the patient is suffering from lupus erythematosus and dermatitis medicamentosa which has altered the pathologic manifestations.

## A Case for Diagnosis (Contact Dermatitis?) Presented by DR J LOWRY MILLER

M B, white woman aged 38, is presented from the Vanderbilt Clinic, where she has been treated for the past two years for recurring attacks of redness involving the nose and the flush areas of the cheeks. The attacks have lasted anywhere from a week to two months. They are not accompanied with elevation of temperature or malaise. A complete medical study revealed only dizziness of unexplained origin, and laboratory tests revealed only a positive reaction for guinea in the stool.

A psychiatric study revealed considerable conflict between the patient and her husband. The patient attributed many other exacerbations of the eruption to her face to this conflict. For several weeks in March 1944 there were lesions present on her scalp which suggested the diagnosis of psoriasis.

The patient presents over the nose and the flush areas of the face a sharply circumscribed red scaling area. The lesion does not have a distinctly elevated border. Lymph nodes of the neck are not swollen. The temperature is 98.6 F.

# DISCUSSION

DR THOMAS N GRAHAM This eruption impresses me as being either a contact dermatitis or a toxic erythema. I think that it might possibly be seborrheic congestiva, which may later develop into lupus erythematosus. The history given by the patient is rather vague.

DR MAURICE J COSTELLO It is difficult for me to get a clear idea of just what this patient had, whether there was clearing between attacks or whether there was considerable erythema during the exacerbation. She said that the eruption reaches its peak within forty-eight hours. As she describes it, it is inflammatory in character. It would be interesting to find out whether effect sulfonamide compounds would have on this eruption.

on It may be an erysipelatous eruption which may eventually lead to solid edema

DR RICHARD J KELLY I questioned the patient as to the duration of the eruption and concerning the original location She insists that it began near the tear duct rather than down in the corner of the nose In my mind that rules out an erysipelatous eruption That was my impression I think that the case still bears investigation The suggestion Dr Costello made about using sulfonamide compounds is acceptable I do not believe that a biopsy would be of any value

DR ROYAL M MONTGOMERY I thought the eruption was of an infectious nature In questioning her, I learned that a flare-up of sinusitis was found to occur with some attacks This fact would warrant a therapeutic trial of the sulfonamide drugs or staphylococcus ovoid

DR J LOWRY MILLER Both diagnoses have been kept in mind over a period of two years The attacks occur anywhere from a week to two months apart, are not accompanied with fever or malaise, and take two or three months to clear A number of patch tests were made with negative results The patient is very emotional The history is unreliable

**Dermatitis Herpetiformis of Unusual Type** Presented by MAURICE J COSTELLO, M D

A R, a married woman aged 41, from Lenox Hill Hospital, outpatient department, has had a localized pruritic eruption on the buttocks and the posterior part of the thighs for two years It consists of numerous broad, linear, crusted excoriations and superficial scarring on a reticulated hyperpigmented background

#### DISCUSSION

DR J LOWRY MILLER I accept the diagnosis of dermatitis herpetiformis If penicillin is available, I advocate its use Patients I have heard about who were treated with penicillin are said not to have had recurrences, as they do when treated with the sulfonamide drugs

DR THOMAS N GRAHAM I believe that the presenting diagnosis is the most probable one, but I think that a biopsy is warranted Since the eruption is sharply margined and since its distribution is so limited, a contact dermatitis from underwear should be considered

DR RICHARD J KELLY I am more in agreement with Dr Graham's statement than with the diagnosis as presented I think it extremely possible that this eruption is a contact dermatitis

DR ROYAL M MONTGOMERY One patient whom Dr Costello presented about two years ago was given sulfapyridine, and her eruption cleared up quickly I have had more success with sulfapyridine than with sulfathiazole or sulfadiazine in cases of dermatitis herpetiformis

DR MAURICE J COSTELLO I think that from a clinical point of view this patient has dermatitis herpetiformis, because of the location of the eruption on the buttocks and because of the superficial scarring, hyperpigmentation and excoriations present in some areas I treated a patient with dermatitis herpetiformis with sulfapyridine, and she has remained free from the eruption to date She had had the disease for six years I think that sulfapyridine is superior to the other sulfonamide compounds but is more toxic than some Physicians have been using 1 to 2 tablets a day for a period of two years, without recurrence In most cases, as soon as one withdraws the drug the disease recurs

I will hospitalize this patient at Bellevue Hospital and try penicillin, if the eruption clears, I will present it at the next meeting

NOTE—After the patient was presented, sulfapyridine was administered in 0.5 Gm doses three times a day for the first week, without improvement The eruption cleared during the following week, when the same dose was administered five times a day

#### MINNESOTA DERMATOLOGICAL SOCIETY

S E SWEITZER, M D, *President*

H A CUMMING, M D, *Secretary*

*Minneapolis, Sept 15, 1944*

**Reticulum Cell Sarcoma** Presented by DR C A W LAYMON, Minneapolis

A C, a white woman aged 59, was admitted to the University of Minnesota Hospitals on Aug 19, 1944 complaining of tumors of the breasts, chest, neck and back beginning in December 1943 and increasing in size and number of lesions since then Mild itching was the only unpleasant symptom The patient had lost 100 pounds (91 Kg) and on admission weighed 209 pounds (94.8 Kg)

Biopsy of bone marrow showed a moderate increase in plasma cells, but the marrow was otherwise normal In the peripheral blood an occasional undifferentiated reticulum cell was present These cells constituted 1% that of a leukemic process at the time of examination The presence of a lymphoblastoma, the pattern was that of a leukemic process at the time of examination The sedimentation rate was 97 mm in sixty minutes Serologic tests for syphilis elicited negative reactions A roentgenogram of the chest showed no evidence of enlarged hilar nodes There was an increase of bronchovascular markings throughout both pulmonary fields

Examination shows an obese woman with nodules on the skin localized to the sides of the neck, upper part of the back, sides of the abdomen or flanks and breasts The nodules are stony hard, some have a more fibrous consistency than others The color varies from bright red, with a waxy translucent appearance, to a deep violaceous red, with the surface resembling an orange peel or pig skin The nodules are in the skin, and so are firmly adherent to underlying tissues They vary from 2 by 3 cm to large plaques with circinate and serpiginous borders, suggesting the coalescence of several individual nodules or irregular growth factors of the individual nodule There are large (walnut-sized) axillary lymph nodes It is impossible to be sure whether there are nodes in the groin, because of obesity, or in the clavicular regions, because of the overlying involvement of the skin The abdomen is covered with a thick pannus adiposus and no enlarged lymphatic organs are palpable

Microscopic sections of one of the nodules fixed in Helly's solution and stained with hematoxylin and eosin were shown

#### DISCUSSION

DR HAMILTON MONTGOMERY, Rochester I am at a disadvantage just glancing at the slides which have been subject to such minute study by various cytologists and others Clinically, this case represents one of mycosis fungoides of the d'emblee type, which histologically usually proves to be small round cell lymphosarcoma but can also be a reticulum cell lymphosarcoma I have

objection to the term "reticulum cell sarcoma" In some cases mycosis fungoides develops into various types of monocytic leukemia or reticuloendotheliosis

DR STURMANS (by invitation) The surprising thing that in looking at this section one sees large capillaries filled with immature cells and that these cells are not apparent in the peripheral blood stream The only thing that makes one suspicious is the fact that the lymphocyte count for this patient is about 50 per cent and there are considerable numbers of reticulum cells which are missing from this reticulum cell sarcoma If the laboratory technician finds a high reticulum cell count in the peripheral blood stream and does not find it thereafter, the one positive finding cannot be discounted

DR L H WINER, Minneapolis I agree with Dr Sturmans in that this patient may at times have had greater numbers of reticulum cells in the blood stream than is shown by the count The differential smear shows only 0.5 per cent reticulum cells The histologic section of the skin shows dilated blood capillaries full of these immature reticulum cells There are periods at which this patient will probably show leukemia in the blood due to breaking through of the immature reticulum cells into the blood stream This patient corresponds to the patient with a reticulum cell sarcoma shown by Dr Sweitzer at a previous meeting These tumors are more like mycosis fungoides clinically I agree with Dr Montgomery that lymphosarcoma is of two types small lymphatic type and the large reticulum cell type Clinically, they look alike, but histologically they are different, even though they are lymphosarcomas Therefore I do not think that clinically one can ever make a diagnosis from the cellular structure of a lymphoblastoma, whether it is small cell or large cell Reticulum cell sarcoma must be determined histologically

DR S E SWEITZER, Minneapolis What about the Sweitzer-Winer test?

DR L H WINER, Minneapolis We tried imprints of the skin, but they were negative

DR S E SWEITZER, Minneapolis I think that this case, being to my notion clinically mycosis fungoides but microscopically reticulum cell sarcoma, simply shows these groups are closely related, they are almost the same thing

DR HAMILTON MONTGOMERY, Rochester Lane of the Skin reported a case of mycosis fungoides associated with Kaposi's sarcoma, and I have an illustration of a case in my chapter in Christian's "Oxford Loose-leaf Medicine" on "Mycosis Fungoides, Lymphoblastoma of the Skin and Allied Conditions as General Diseases" in which the patient clinically showed typical mycosis fungoides as did the sections from the skin, whereas biopsy of the lymph node revealed lymphosarcoma of Hodgkin's type and the blood picture was that of lymphatic leukemia

DR L H WINER, Minneapolis That is the point large Sweitzer and I are attempting to make In a lymphosarcoma, there may be a lymphatic leukemia picture in the blood when the proliferation breaks into the blood stream and throws its cells into the circulating blood This gives a picture of lymphatic leukemia in the blood and is frequently found just before the patient's death in lymphosarcomas

DR S E SWEITZER, Minneapolis That is not a pertinent picture

DR CARL LAYMON, Minneapolis The close relationship between these various conditions has been emphasized It has also been claimed by some observers that

mycosis fungoides of the d'emblee type is different from mycosis fungoides of the usual type The 3 cases of the former which I have had could have been lymphosarcoma clinically, yet the sections were identical with those from mycosis fungoides of the usual variety

**Mycosis Fungoides** Presented by DR HENRY E MICHELSON, Minneapolis

G W, a white man aged 56, first noted a growth on the lobe of the right ear three months ago This increased gradually in size There were no other visible lesions on the body

Examination shows a cyanotic tumor of the lobe of the right ear The tumor has a firm consistency and is painless It is 2 cm in diameter

Histologic sections were shown

#### DISCUSSION

DR S E SWEITZER, Minneapolis Did the patient have any injury to the ear?

DR HENRY E MICHELSON, Minneapolis Yes, he had an injury but not a hematoma

DR S E SWEITZER, Minneapolis It looks inflammatory to me

DR CARL LAYMON, Minneapolis It is difficult for me to ascribe the nodules that Dr Michelson mentioned to injury to the ear It looks to me as though the disease will eventually turn out to be malignant

**A Case for Diagnosis (Parapsoriasis?)** Presented by DR CARL LAYMON, Minneapolis

H M, a white woman aged 25, was first seen on Sept 8, 1944, complaining of an eruption on the trunk, thighs and legs She stated the first attack appeared in February 1944 and lasted five or six weeks, with complete involution of the eruption The eruption appeared again in July, only on the legs, and cleared in a few days The eruption reappeared by August 10 and has continued to this time

Examination shows a patchy distribution over the trunk, thighs and legs, the face, palms and soles are free The lesions are macules varying from 1 to 3 cm in diameter and are covered with a light scale The color is fawn Some of the lesions are oval with the long axis in the line of cleavage in the skin

Results of serologic studies for syphilis were negative Histologic sections were shown

#### DISCUSSION

DR C W LAYMON, Minneapolis I suppose that every one who saw the patient thought of the same possibilities that my colleagues and I did, namely, parapsoriasis, pityriasis rosea and seborrheic dermatitis The scalp is relatively clear The eruption is persistent, with some remission since last February, which is against pityriasis rosea A histopathologic section was against parapsoriasis, it fitted in more with pityriasis rosea

DR S E SWEITZER, Minneapolis I think that, clinically, it is pityriasis rosea that has been washed Such patients can be cured if they can be made to quit washing

DR HAMILTON MONTGOMERY, Rochester The histologic structure of parapsoriasis is not diagnostic, and in the guttate forms one might see migration of leukocytes throughout the epidermis, forming small microabscesses, similar to that seen in pityriasis rosea Therefore, the diagnosis should be decided on clinical rather than on pathologic grounds

### Nevus Unius Lateris Presented by DR S E SWEITZER, Minneapolis

G S, a white woman aged 28, has an eruption which has been present since birth. It is situated behind the right ear. The patient stated that it enlarged recently.

Examination reveals a papular, dull red eruption behind the right ear. The top of the papules are of a waxy white color, and there is one plaque measuring about 3 by 2 cm. This lesion clinically strongly resembles nevus sebaceous of Jadassohn, but the microscopic examination shows it to be nevus unius lateris.

Histologic sections were shown.

#### DISCUSSION

DR S E SWEITZER, Minneapolis. Clinically, the lesion looked like nevus sebaceous, but a biopsy showed that it was not that.

### A Case for Diagnosis (Bullous Eruption?) Presented by DR S E SWEITZER, Minneapolis

M A, a white linotype operator aged 77, entered the Minneapolis General Hospital because of blisters on both legs. About two months ago a small blister was noticed on the lower third of the left leg. As it enlarged, others developed. The lesions did not itch and lasted about three weeks. Except for sponging the legs with magnesium sulfate solution, no internal or topical medications were used prior to admission. His previous health was good.

Laboratory tests showed hemoglobin content, 96 per cent, leukocytes, 8,000, neutrophils, 67 per cent, lymphocytes, 72 per cent, monocytes, 8 per cent, and eosinophils, 3 per cent. The urine was normal, and serologic tests for syphilis elicited negative reactions. The blood urea nitrogen level was 15 mg and the chloride level 678 mg per hundred cubic centimeters.

On the lower half of each leg there are ten to twelve bullae in various stages of involution. The bullae measure 2 to 4 cm in diameter, contain a nonpurulent fluid and are on a noninflammatory base. The blisters shrink and dry in situ. Nikolsky's sign is not elicited. While the patient was in the hospital two new lesions developed.

Histologic sections were shown.

#### DISCUSSION

DR HAMILTON MONTGOMERY, Rochester. Histologically, there are distinct vesicles and bullae, but there is more inflammatory reaction than one would expect to see in an ordinary pemphigus. There is a decided eosinophilia in the tissue, which would fit in with either pemphigus vegetans or dermatitis herpetiformis. Clinically, I thought of a fixed drug eruption but could obtain no history of any medication. I do not think the case is one of pemphigus, but I believe that it is rather an instance of a bullous toxic dermatitis, probably on the basis of a dermatitis medicamentosa.

### Dermatitis Herpetiformis Presented by DR S E SWEITZER, Minneapolis

F F, a Chinese laundry worker aged 73, was said by an interpreter always to have been in good health but that two years ago he began to have a generalized itching. No cutaneous lesions were noticed until blisters began forming about two months ago. There was no history of ingestion of drugs. Circinate erythematous plaques were present at the onset of the eruption.

Examination reveals an emaciated Chinese man. A large portion of the body is involved with a patchy dark

brown pigment. The face, the upper part of the back and the calves are relatively free. On the periphery the patches vesicles are present, and on the feet a lower part of the legs bullae are present. The itching is severe. The patient has been receiving 3 Gm sulfapyridine daily for the past four weeks, and attempt to discontinue use of sulfapyridine was followed by an increase in the number of vesicles. A patch with 50 per cent potassium iodide ointment elicited negative reaction.

The hemoglobin content was 91 per cent, erythrocytes, 4,900,000, and leukocytes, 6,300, with neutrophils 50 per cent, lymphocytes 20 per cent, monocytes 2 per cent and eosinophils 28 per cent. Urinalyses gave normal values, and serologic tests for syphilis elicited negative reactions. The blood urea nitrogen content was 14 mg, the blood chloride content 644 mg and the blood calcium content 9.9 mg per hundred cubic centimeters.

Histologic sections were shown.

#### DISCUSSION

DR L H WINEY, Minneapolis. It is an interesting case to us because Dr Sweitzer and I had the patient in the hospital about four weeks ago and treated him with sulfapyridine and the lesions cleared up. Within four days after his discharge, without sulfapyridine the eruption recurred and he had to be readmitted to the hospital. He now had multiple bullae the size of a walnut on his feet and on his scapula and trunk. We prescribed sulfapyridine, and within a period of three or four days the bullae dried up and the man became much improved. We then stopped the sulfapyridine and the bullae recurred. We again prescribed sulfapyridine, and three days ago we stopped it, in order that there might be bullae to show you today, but they did not break out. Then we gave him potassium iodide by mouth but it did not produce any bullae.

### Generalized Progressive Scleroderma Presented by DR CARL LAYMON, Minneapolis

Mrs L W, aged 39, was first seen in the University of Minnesota Hospitals on Sept 13, 1944, complaining of dark brown pigmentation of the skin, stiffness of the joints of the wrists, fingers, shoulders, knees, ankles and toes and tightening of the skin slowly progressing over one year. The disease began as an infection of the upper respiratory tract, pigmentation was first noted about January 1944. The disease has slowly progressed from the time of onset to the present.

Examination shows generalized deep brown pigmentation with white striations of the chest, acrosclerotic watch crystal nails and extreme limitation of motion of the fingers, wrists and toes, with some limitation of motion of the shoulders, ankles and knees. The skin of the fingers and forearms is tense and indurated but is not painful.

Histologic sections were shown.

#### DISCUSSION

DR CARL LAYMON, Minneapolis. The question came up about the possibility of dermatomyositis, but in the absence of eruption other than pigmentation and absence of muscular atrophy made us believe it was generalized scleroderma. The patient did not have heliotrope-colored eyelids that frequently are noted in dermatomyositis.

DR HAMILTON MONTGOMERY, Rochester. I have seen severe generalized pigmentation in association with generalized scleroderma to the extent that internists have made an erroneous diagnosis of Addison's disease.

Dr J F MADDEN, St Paul A patient with acute dermatomyositis in my service at the Ancker Hospital responded favorably to penicillin

**Morphea** Presented by Dr S E SWEITZER, Minneapolis

H D, a white woman aged 36, first noticed an eruption consisting of white spots in the left midclavicular region four years ago. There was a slow progression in the size of the lesions. A diagnosis of syphilis was made elsewhere in 1926, and she stated that she received two years of continuous treatment. She had an acute dacryocystitis in May of this year.

Examination reveals a patch 5 by 3 cm over the left axilla. The patch is made up of numerous elongated white shiny macules. The skin is atrophic in this area. Serologic tests for syphilis elicited negative reactions, hemoglobin blood counts and results of urinalyses were normal. The basal metabolic rate was -3 per cent, the blood urea nitrogen level was 11 mg, the uric acid level was 4 mg, and blood chloride level was 660 mg, per hundred cubic centimeters.

Histologic sections were shown

## DISCUSSION

Dr L H WINER, Minneapolis The reason for showing this patient is that we thought that her case complicated that of a patient whom Dr Montgomery showed at the meeting a year ago in Rochester, where a question came up regarding the differential diagnosis of lichen sclerosus from morphea clinically. This patient's eruption resembles lichen sclerosus clinically, but a diagnosis of morphea is definite histologically.

**Lupus Erythematosus with Metastases to the Right Inguinal Nodes** Presented by Dr C LAYMON, Minneapolis

W K, a white man aged 76, was first seen on August 1944, complaining of painless warty growths on the back of twelve years' duration. The central lesion has grown more rapidly in the past few months.

Examination shows numerous crusted, elevated lesions on the lumbar region of the back. One is a bright red, elevated firm nodule 2 by 3 by 1 cm. The inguinal lymph nodes on the right are 4 by 10 cm and are hard.

Serologic reactions for syphilis were negative.

Microscopic sections were shown

## DISCUSSION

Dr HAMILTON MONTGOMERY, Rochester This case fulfills the clinical and histologic requirements for Bowen's disease. Clinically, there is arciform configuration, and histologically there is a squamous cell epithelioma in situ, although several of the sections show an invasive, highly malignant squamous cell epithelioma, grade 4. Bowen's precancerous dermatosis can remain for many years as such, clinically benign but histologically a squamous cell epithelioma in situ, but it may suddenly show malignant invasion, as is occurring in this case.

**Chronic Lupus Erythematosus, with Reticulation of the Forearms** Presented by Dr L H WINER, Minneapolis

Mrs H L aged 33, was first seen in July 1942, and a diagnosis of lupus erythematosus of the discoid type involving the face was made. After treatment with

gold sodium thiosulfate intravenously and bismuth subsalicylate intramuscularly, the lesions faded out completely by December 1942. In February 1943 she had bilateral hidradenitis suppurativa which responded to roentgen ray therapy and wet dressings. In May 1944 lesions developed on the sides of the face and on the neck, arms and forearms. These lesions were erythematous sharply outlined plaques. After treatment with bismuth subsalicylate, the lesions on the face disappeared, but those on the arms and forearms remained.

Examination shows a definite reticulated eruption on both forearms and arms. The lesions on the face have completely regressed except for the erythema, which is still evident on the cheeks. This erythema can be expressed by diascopic pressure. There is a fine scale on the lesions on the forearms.

Microscopic examination of tissue removed from a lesion on the forearm shows epidermal atrophy, follicular hyperkeratosis and nests of round cell infiltrate in the cutis. The section is comparable with a diagnosis of lupus erythematosus.

Histologic sections were shown

## DISCUSSION

Dr HAMILTON MONTGOMERY, Rochester From the history this patient may well have had lupus erythematosus, but she presents insufficient clinical or histologic evidence at the present time to warrant such a diagnosis. The sections lack many of the features that are necessary for a histologic diagnosis of lupus erythematosus, and they fail to show liquefaction degeneration of the basal layer, keratotic plugging and other features.

Dr L H WINER, Minneapolis Two years ago this patient had discrete subacute lupus erythematosus which responded to treatment with bismuth and later with gold and clinically was entirely cleared in six months. She came back this spring with recurrence of the lupus erythematosus on the face and also reticulated lesions on the forearms. The latter resembled erythema multiforme so much that I prescribed sodium salicylate. There was no response to the salicylate in two weeks. I then treated her with bismuth intramuscularly and the lesions on the face and arms disappeared completely except that on the arms reticulation was left. This reticulation sometimes is so faint that one cannot see it. Today it did not show as well as it does at other times. I am of the opinion that this histologic section agrees with the histologic picture one sees in lupus erythematosus. I could see atrophy of the epidermis, follicular plugging and round cell infiltrate in the cutis.

Dr S E SWEITZER, Minneapolis I have seen a similar case, that of a young woman with definite lupus erythematosus on the face which was chronic. There were no lesions on the body. She went outdoors and hung up clothes for a short time in the sun, and a similar eruption developed on her arms. She began to have fever, and I put her to bed, she recovered, and did not have any after-effects, the disease disappeared in four to six weeks. Hence it was a case of subacute lupus erythematosus developing from sunlight.

Dr HAMILTON MONTGOMERY, Rochester I thought that this patient presented rather a picture of livedo reticularis with a histopathologic picture consistent with this or with a toxic dermatitis.

Dr L H WINER, Minneapolis A Mantoux test (1:1,000) elicited a negative reaction.

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## TYPES OF DERMATITIS IN AMERICAN ONCHOCERCIASIS

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IN A previous communication<sup>1</sup> the general background of American onchocerciasis was given. In this report an attempt will be made to describe in detail the different forms of dermatitis that were observed, for the most part, at the research center of onchocerciasis, Centro Médico, Huixtla, Chiapas, Mexico. This research hospital has been placed in the state of Chiapas in an area in which onchocerciasis is heavily endemic. The incidence of the disease here has been estimated at 20,000 by González Herrejón.<sup>2</sup>

It is difficult to analyze critically the cutaneous reactions observed in patients infected by the filariae worm, *Onchocerca volvulus*, for the following reasons:

1 Many areas of skin, structurally normal, grossly and even microscopically, and also free of subjective reactions, may show numerous microfilariae in that portion.

2 The vector of the disease, the *Simulium*, produces an erythema-edema and petechial reaction, with the intensity of the cutaneous changes varying according to the sensitivity of the person. Furthermore, one may suffer many bites at frequent intervals in adjacent areas.

3 Although much work is being done on the immunobiology of onchocerciasis, as yet no definite and absolute method has been found to

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1 Goldman, L. American Onchocerciasis, *Arch. Dermat. & Syph.* 50:385 (Dec.) 1944.

2 González Herrejón, S. Estado actual del problema de la oncocercosis en la República Mexicana, *Bol. Of. San. Panam.* 15:735, 1936.

determine the degree of sensitivity of the skin and subcutaneous tissues of the person to the presence and activities of *Onchocerca volvulus*

4 Pruritus, with its associations of secondary coccid and mycotic infections, is always a disturbing and complicating feature in tropical and subtropical peoples, and this reaction is present in many patients with onchocerciasis

5 The associated factors of avitaminosis and intestinal parasitism, especially uncinariasis, are very common

6 It is not possible as yet to reproduce the same disease under controlled conditions in experimental animals

7 There is no specific therapy at present

However, in spite of these objections, from the clinical observations of those who have had considerable experience with this disease in Guatemala and Mexico, it is possible to list a number of certain cutaneous reactions which are seen in patients with American onchocerciasis and which are apt to disappear or improve after amelioration of the onchocercal infection in the patient. Mention was made previously of the classification of onchodermatitis by Diaz,<sup>3</sup> namely the edematous, chromatic, dry glossy (*lustroso*) pruriginous and mixed

The commonest cutaneous reactions that were observed in patients with onchocerciasis at Centro Medico in Huixtla may be classified as follows

1 Reactions associated directly with the onchocerciasis

(1) Subcutaneous nodules

(2) Dermatitis

A *Mal de morado* or *dermatosis pigmentada onchocercosa*

B Localized edemas (elephantiasis), acute and chronic

C Forms of lichenification

D Acute subacute and chronic eczematoid dermatitis with or without pyoderimas

(3) Reactions to the bite of a simuliid

(4) Scarring from cutaneous biopsies or excision of nodules

(5) Dermatitis from therapeutic agents

2 Nonrelated cutaneous conditions in patients with onchocerciasis (a partial list)

(1) *Mal del pinto*

(2) Mycoses

(3) Ulcers of the leg

(4) Syphilis

3 Diaz, A. F. Onchocercosis de Robles, Bol. san. Guatemala **14** 118 (Jan-Dec) 1943



Of course, many other forms of cutaneous reactions have been described, even in the important group of onchodermatitis, but the aforementioned classification emphasizes the commoner clinical types

Since some controversy concerns the differentiation between the bites of the insect vector and onchodermatitis per se, it is important to review the reaction to the bite of the black fly, the *Simulium*. Luis Vargas<sup>4</sup> has made some important contributions in this field. The maxillas of the black fly serve, as many investigators have indicated, as a type of scissors, and the proboscis of the fly is introduced into the pars papillaris (exact locus?) Injection of saliva of the insect and an anticoagulant substance is then made. The reaction to the local trauma, the saliva and the anticoagulant cause destructive changes both in the epidermis and in the dermis. If the *Simulium* is infected, the infective larval form of *Onchocerca volvulus* passes through the proboscis into the upper part of the dermis. According to Vargas, the exact form of this infective type in the skin and its migrations and development subsequently until the formation of the encysted nodule, containing adult worm or worms, are unknown. Moreover, the *Simulium* also attracts a considerable number of microfilariae present in the person into the area of its bite, and these forms may be taken up during the ingestion of blood by the *Simulium*. Relatively few of these larvae so ingested complete their development eventually in the thoracic musculature of the fly. The essential clinical elements of the bite of a simuliid are then pruritus, central petechial hemorrhage and edema. The edema may subside in several days but the discoloration from the petechial hemorrhages may persist for some days or even weeks and the pruritus usually continues for four to five days. In a hypersensitive patient, of course, the reactions, especially the edema phase, are intensified. Under field conditions, especially among the natives, persons are bitten frequently by large numbers of the simuliids. As a result of the pruritus, secondary infection may occur, and there are produced excoriations, pyodermas, especially of the impetiginous type, scarring areas and depigmentation, especially prominent in dark-skinned persons. In bites on the lower extremities, the petechial reaction and its subsequent hemosideric phase may be severe. Histopathologic study of a late reaction to a bite in a person not clinically hypersensitive revealed slight epidermal changes, essentially of thinning, vacuolation and pyknosis and some edema of the papillae with scattered lymphocytic infiltrate, chiefly perivascular. Occasional plasma cells and eosinophils were noted. It is not possible at present to say that clinically or even histologically the cutaneous reactions to a bite of a noninfected simuliid is different from the reaction to that of a simuliid carrying microfilariae. The degree of the reaction is supposed to vary according

4 Personal communication to the authors



to the sensitivity of the person to the Simulium. As yet, this has not been established by cutaneous tests with Simulium extract or other substances. Of course, increased local heat (increased blood supply?) and increased sweating accentuate the degree of the reaction to the bite. An important part of the campaign against onchocerciasis has been the attempt to educate the natives to wear clothes to cover most of the body during the day. According to Vargas, mosquitoes and ticks (*garapates*) may ingest the microfilariae of *Onchocerca volvulus*. Here also, it is not possible to tell differences between bites of infected and noninfected insects. The modern advances in the field of chemical control of insects by mass protection with such agents as pyrethrum and DDT (dichlorodiphenyltrichloroethane) mixtures and individual protection by repellents and DDT can do much to control these vectors with certain selective groups.

It may be possible<sup>4</sup> in the future, by means of quantitative dilutions of the cutaneous test antigens and the complement fixation tests to follow the course of onchocerciasis. At present, the practical method is to perform repeated biopsies of the skin to determine the viability of the adult worms in these nodules. In addition, clinical changes in the skin and also in the eyes may be used to follow the progress of the disease. In the Mexican series, epilepsy was found in approximately 10 per cent of the subjects according to records. The significance of this reaction in onchocerciasis remains to be studied in a more critical fashion.

Moreover, for patients who are under detailed observation over a period of time, it may be necessary to perform frequent biopsies. Work is being done to attempt to standardize biopsies since negative reports may not be absolute in that a biopsy repeated in the same area at another period may reveal many microfilariae. Because the bite of a simuliid has the power to attract microfilariae, an injection of Simulium extract (or even histamine?) may be of some help. Areas of dermatitis are no more or less certain to show microfilariae on biopsy than are areas of normal skin. The biopsy sites include usually the cheeks, neck, forearms and thighs and occasionally the palpebral conjunctivas. Although the method of obtaining the specimen for biopsy consists in shaving off a small portion of the skin through the upper part of the corium, small depigmented areas in the skin of a mestizo patient may remain, and a number of these may accumulate during the year. A keloidal reaction has not been observed in these biopsy sites, although it has been observed in the scars of excision of onchocercomas.

Reactions to therapy may include dermatitis from the local use of antipruritic remedies, the local use of filaricidal (especially microfilaricidal) agents and the parenteral use of arsenicals, mercury and antimony salts. As a rule, the sensitivity reactions to mercury, especially mercuric cyanide, used originally for injections into the oncho-

cercomas, and to anthiomaline (lithium antimony thiomalate) were reported as being rare

The characteristic nodules (onchocercomas) have been described in a previous communication<sup>1</sup> In Mexico, extensive and detailed histopathologic studies of the nodule have been made by Manuel Martínez Báez<sup>5</sup> His studies and the recent ones of Germain<sup>4</sup> with the use of silver impregnation stains have contributed much to the knowledge of the pathology and even of the pathogenesis of this disease The distribution of the nodules observed in Mexico differed somewhat from that in Guatemala A review of 100 records at Centro Médico revealed the following distribution of nodules

Head	40
Neck	6
Upper part of trunk	15
Iliac crest	7
Upper extremities	2
Lower extremities	9
Site not stated	21

Additional information in regard to the mechanism of the nodule formation has been suggested by Ochoterna,<sup>6</sup> who claimed that the "first beginning of the formation of the onchocercous cyst is provoked by the obstruction of the lymphatic passages" (proof?) This is of interest in relation to another filariae worm, *Wuchereria bancrofti* Some nodules may contain only males, and these nodules, of course, are nonproductive in regard to microfilariae A number of cases of new onchocercomas recurring next to the scar, in the scar and even below the scar of a previous extraction of onchocercomas were seen No systemic reactions, so-called crises, following surgical removal of the nodules, were observed in a group of 6 patients

The dermatologist is familiar with the local dermatitis from the penetration and invasion of the skin by certain helminthic larvae These worms produce reactions which include especially the erythematous, papular and urticarial lesions of cercarial dermatitis, the pruritic, papular, vesicular and tunneling lesions of the hookworm larvae and the petechial, pruritic and infected lesions of *Strongyloides* larvae A more detailed study of these common larval infections of the skin and their local sensitivity reactions would do much to help one understand the cutaneous reactions to the penetration and migrations of the filarial worms in superficial tissues In filariasis caused by *Wuchereria ban-*

5 Martínez Báez, M Sur la structure histologique des nodules à *Onchocerca volvulus* et à *O. caecutiens*, Ann de parasitol 13 207 (May 1) 1935

6 Hoffmann, C, and Vargas, L. Nuevas comunicaciones acerca de la onchocercosis de Chiapas, in Memoria del III Congreso de la Asociación Médica Panamericana, Mexico, 1933, p 777

crofti, Napier <sup>7</sup> has asserted that some of the natives have localized but transient pruritic nodules. As has been mentioned before, for onchocerciasis, little is known of the stage from the entrance of the infective larval form to the development of the adult stage.

When a person harbors adult worms in onchocercomas, certain cutaneous reactions occur. Martínez Baez <sup>5</sup> believes that those persons with poor nutrition and poor personal hygiene are more apt to show cutaneous manifestations. One of the most interesting, and incidentally most confusing, types and one of the most difficult for the inexperienced observer to diagnose is the *mal de morado* type. Prior to the study of Huixtla, one of us (L. G.) had never seen a case or could be certain of a true *mal de morado* and had difficulty in learning to recognize it in the mestizo patients. However, the patients themselves could find the disease with ease. In *mal de morado*, the skin is usually smooth, occasionally dry or wrinkled and not hot and presents a peculiar reddish or bluish red or purplish (*morado*) and sometimes even greenish discoloration. Edema may or may not be associated. Biopsy in a case of this type revealed only slight epidermal changes with no increase in melanin pigmentation, moderate perivascular lymphocytic infiltrate and some edema and separation of the collagen fibers. A few microfilariae were found scattered in the upper portion of the dermis. No chromatophore pigment was observed. No bacteria were seen. Tissue was not cultured for organisms. The records of 38 patients receiving diagnosis of *mal de morado* at Centro Medico were reviewed. Most of them had had nodules. The majority of the cases of *mal de morado* appeared within three years after the first appearance of onchocercomas. The distribution of *mal de morado* was as follows:

Cheeks	26
Nose	1
Ears	10
Arm	1 (nodule present also in this area)

Fifteen of the patients complained of pruritus, 3 of increased local temperatures and 4 of "biting sensation." In some cases the *mal de morado* disappeared partially, in other instances completely, after excision of palpable nodules. Without excision the *mal de morado* appeared to persist for many months (average duration?). Biopsy specimens from the face are usually positive for microfilariae, show no increase in melanin and no chromatophore pigment and show some perivascular infiltrate. In the absence of any detailed investigative studies of local blood flow, cutaneous temperature, bacterial cultures and his-

<sup>7</sup> Napier, E. Filariasis Due to *Wuchereria Bancrofti*, *Medicine* **23** 149 (May) 1944.

tamine whealing, one can guess only that the changes of color are due to disturbances in blood supply through vasodilation and some lymphedema, possibly from a vascular (capillary endothelium and lymphen-

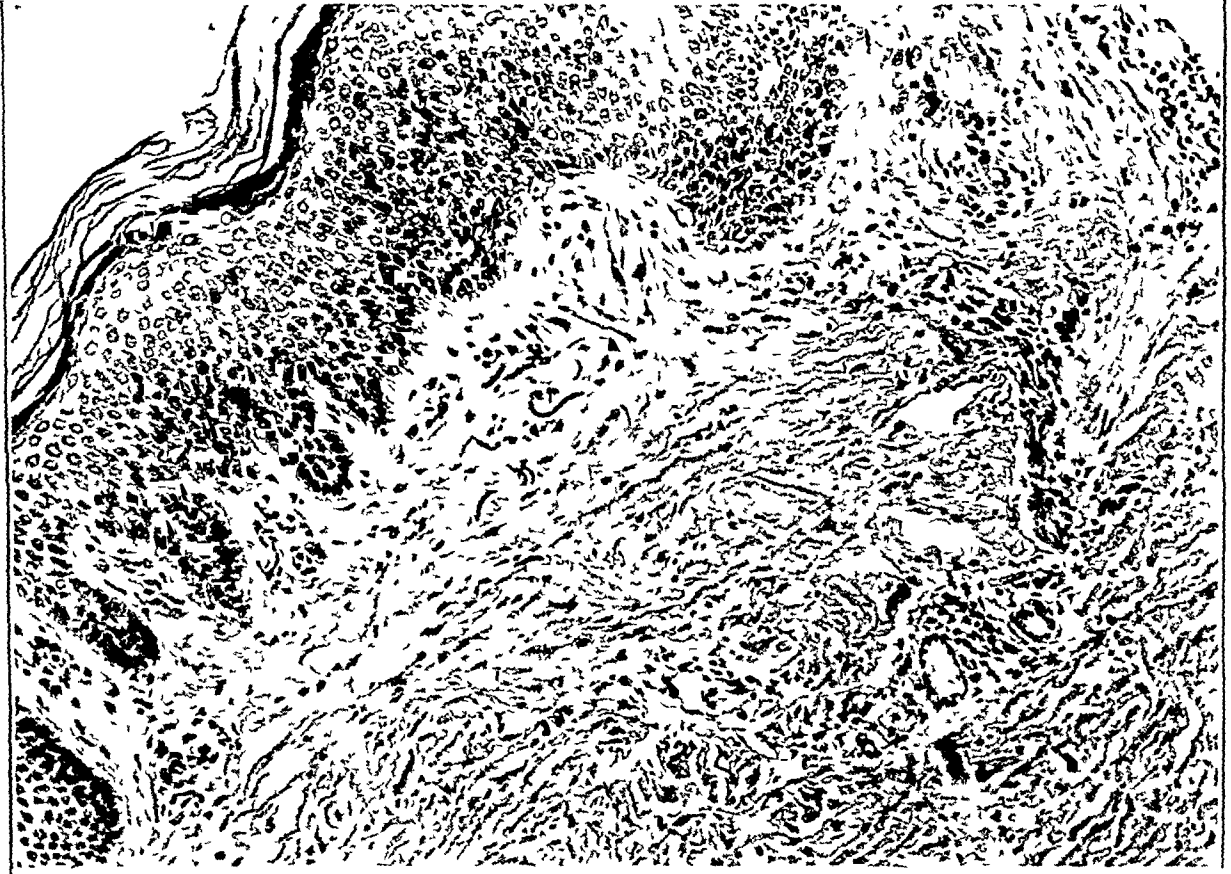


Fig 1—Biopsy specimen from shoulder of a young child with lichenification of face and of shoulder areas. Many microfilariae are present. There are thickening and fragmentation of collagen fibers and perivascular lymphocytic infiltrate. Hematoxylin and eosin,  $\times 120$ .



Fig 2—Onchocerciasis with chronic edema of face of one year's duration. The superficial cutaneous lesions are those of flat warts.

dothelium) allergy Then, *mal de morado* may be considered in the Díaz<sup>3</sup> classification as the "chromatic type"

Frequently associated with *mal de morado* is the edema reaction It is the edema which makes for the onchocerciasis facies, the puffiness about the eyes and the eosinophilia reminding one of a patient with trichinosis In most instances the edema is chronic and appears like myxedema, but occasionally this reaction may be acute and resemble



Fig 3—Biopsy specimen from face of patient in fig 2, showing thinning of epidermis, microfilariae, some separation of collagen fibers with fluid and perivascular lymphocytic collars Hematoxylin and eosin,  $\times 120$

in appearance angioneurotic edema In 20 patients with the edema reaction the location of the edema was as follows

Face, including cheeks, eyelids and ears	16
Trunk	2 (in one the breast was involved)
Lower extremity	1
Hands	1

In only 2 of these patients were no nodules found Complaints of pain and heat were occasionally made In biopsy studies of a patient with unilateral chronic edema of the right thigh, an inflammatory reaction was found to extend deep into the fat tissue with considerable perivascular infiltrate No endovascularitis was made out An occa-

sional microfilaria was found in the upper part of the dermis but none in the deeper tissues. It is apparent that the edema reaction in onchocerciasis indicates a vascular reaction with increased fragility of the vessels or with loss of fluid from increased intravascular pressure through obstruction. In this type of edema the onchocerciasis shows some definite relationship to bancrofti filariasis. In none of the sections studied was there any evidence of epithelioid cell granulomatous reaction such as has been reported to occur in lymphatic tissue infected with



Fig 4—Biopsy specimen showing deep extension of inflammatory infiltrate into fat tissue. An occasional microfilaria was present in the upper portion of the dermis. Van Gieson stain,  $\times 40$ .

*Wuchereria bancrofti*. No endovascular parasites were observed in any of our cases although Vargas<sup>4</sup> indicated that *Onchocerca volvulus* may be found rarely in the blood stream and even in the lymph node. In the absence of bacteriologic studies no help can be offered to the controversy regarding the mechanism of elephantiasis with bancrofti. In a biopsy of a child with edema of the face, without *mal de morado*, of one year's duration the epidermis was normal but thinned. There was some perivascular infiltrate chiefly of lymphocytic type. Microfilariae

were found in the pars papillaris. With the special silver impregnation technic, Germain could demonstrate none in the perivascular spaces or in the perivascular lymphocyte collars. There was no endothelial reaction. There was edema of the dermis with some separation of the collagen. The collagen fibers themselves showed no decided changes on special staining. The skin appendages and subcutaneous tissue showed no changes.

The next characteristic form of chronic onchodermatitis is lichenification. This form involves chiefly the face, where it may be mixed with eczematoid reactions, the extensor surfaces of the arms and forearms and occasionally the thighs and legs. The skin is thickened diffusely, hyperpigmented and intensely pruritic. Three patients with this form of dermatitis were studied in detail. In all of them there were no signs of lichen planus or of cutaneous changes suggestive of a vitamin A deficiency. Moreover, with the limited facilities available, these cases did not seem to reflect any profound psychosomatic reactions. In each patient the cutaneous changes were followed by a period of pruritus. One of these patients had microfilariae in the lichenified areas and also in the normal skin of the shoulder but not in the cheeks. In this patient, no nodules were palpable, and none had been present for more than nine months, although previously a total of twenty-seven nodules had been removed. Anthiomaline (lithium antimony thiomalate) over a prolonged period had no effect on the lesions of the skin or on the microfilariae. Another man, seen as an outpatient, had no nodules and had received no therapy. His young son had onchocerciasis also. The third patient also had microfilariae in the skin and no nodules at present, although he had had nodules on the scalp excised in previous years. None of these patients had received any intensive local therapy. With the lichenified forms an effort was made to determine at what level microfilariae first could be detected. Shavings were made of the lichenified spots and then cut in half. One half was examined directly in saline drop on a slide and the other in fixed section. When the shaving of the slice of skin reached into the superficial portion of the pars papillaris, then microfilariae were seen. Martínez Baez<sup>4</sup> has found microfilariae even among the deeper layers in the epidermis. It has been stated<sup>8</sup> that in the Congo the pruriginous and xerodermatous forms of onchodermatitis were more common than in Guatemala (and Mexico?).

The last type of onchodermatitis was the eczematoid dermatitis reaction. Without special studies, as regards sensitivity to *Simulium*

8 Strong, R. P., Sandground, J. H., Muñoz Ochoa, M., and Bequaert, J. C. Onchocerciasis with Special Reference to the Central American Form of the Disease, Contribution 6, Department of Tropical Medicine and Institute for Tropical Biology and Medicine, Cambridge, Mass., Harvard University Press, 1934.



and perhaps to bacteria and even to *Onchocerca volvulus*, the background of this group could not be determined. These papulovesicular crusted, excoriated, lichenified and at times impetiginized lesions occurred over the extensor surfaces of the arms, legs and thighs. Similar reactions were observed in natives without onchocerciasis. Goems<sup>9</sup> in 1938 described "tropical ulcer type lesions" in San Salvador which presented

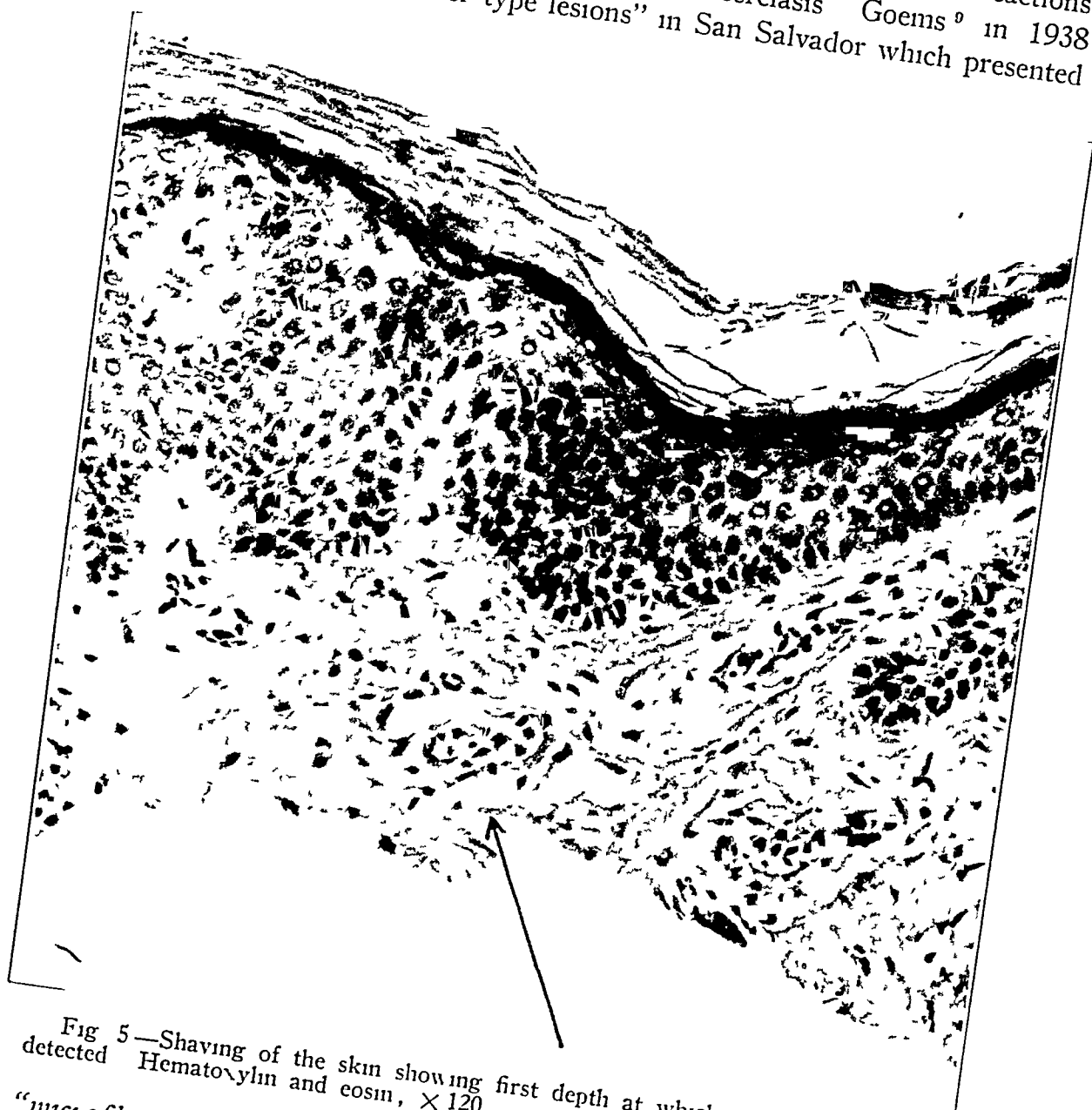


Fig 5—Shaving of the skin showing first depth at which microfilariae were detected. Hematoxylin and eosin,  $\times 120$

"*microfilarias tipo oncocerca*" and also papillomatous verrucous and hyperkeratotic forms on the dorsa of the hands, forearms and neck, all of which showed larval forms of the *Onchocerca* type. No such cases were seen in Guatemala or Mexico by us. In the series of cases

<sup>9</sup> Goems Rosales, A. Oncocercosis, Bol. san Guatemala 5 1 (Jan-Dec) 1938, abstracted, Bol. Of san panam 18 775, 1939

reviewed at Huixtla, there were two tropical ulcers. No notes were made, however, as to the presence of microfilariae in these ulcers.

Some of the other conditions associated with onchocerciasis included urticaria (1 case), *mal del punto* (many cases), "pellagroid" manifestations (1 case), cutaneous syphilis (15 cases), bone syphilis (1 case), varicella (1 case) and pyogenic abscess (2 cases), not related to onchodercomas.

Although among the hospital patients themselves a careful search was made for typical cutaneous reactions of avitaminosis, such as pellagrous dermatitis, glossitis and ariboflavinosis, none could be found. The data with respect to possible avitaminosis from vitamin A are more suggestive. Many of the patients, especially the children, had follicular keratoses.



Fig. 6—Onchocerciasis with depigmented excoriated eczematoid reaction (reaction to bite of a simuliid?).

In the new case history form now available from the Secretaría de Salubridad y Asistencia, Dirección de la Campaña Contra la Onchocercosis en el Estado de Chiapas, detailed questions regarding dietary intake and detailed tabulations of forms of cutaneous reactions are now available. With these excellent forms it will be possible soon to evaluate critically the influence of avitaminosis. It is hoped also that one will be able to apply the microchemical technic of Lowry<sup>4</sup> for vitamin A, especially in those cases of dermatitis with lichenifications, follicular keratoses and diffuse dryness of the skin.

The other important factor in the pathogenesis of the cutaneous reaction in onchocerciasis is the lack of definite information for estimating the tissue response of the patient to the presence of *Onchocerca volvulus*. Previous mention<sup>1</sup> has been made of the reports of quantitative dilutions of antigens for cutaneous tests and also for complement fixation tests. When it will be possible to prove that certain forms of dermatitis are associated with cutaneous hypersensitivity to the filaria the reason for the absence of cutaneous reactions in some infected persons may be understood.

With recent developments in staining technics, especially of the silver impregnation method of German,<sup>4</sup> it may be possible to study

the relationship of the position of the worm to the lymphatic vessels of the skin, especially to their "perivascular passage-channels"

It is hoped that some of the newer technics such as the use of radioactive tracers and also the injections of fluorochromes into onchocercomas may help one to follow the course of the microfilariae Lark-

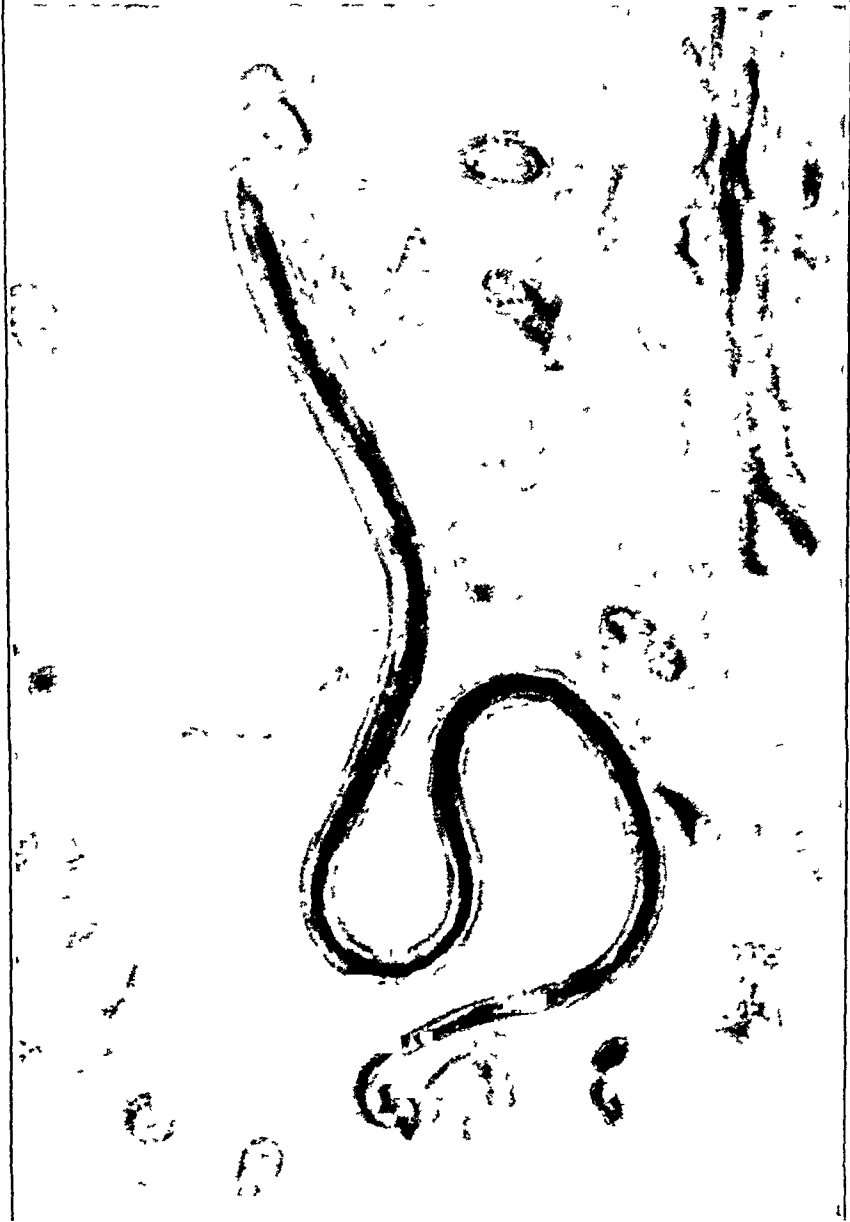


Fig 7—Microfilaria of *Onchocerca volvulus* stained by silver impregnation technic of Germain, showing internal structure and striated pellicle Silver stain,  $\times 480$  (approximately) From the collection of W McKee Germain

Horovitz<sup>4</sup> has expressed the belief that "if tracers are injected into nodules, their presence in adjacent tissue is not necessarily indicative of transport by the microfilariae but can be due to absorption of the tracers by the tissue" He indicated that "more would have to be known

about the metabolism of the organism involved to suggest a tracer technic which would guarantee that the tracer stays with the organism and cannot be exchanged with the surrounding tissue" The capillarscope was not effective in finding microfilariae of *Onchocerca volvulus* in the skin. Examinations for *Wuchereria bancrofti* were not attempted with this instrument. Further studies in the field of cutaneous microscopes, especially with the combined use of fluorochromes and fluorescent lighting, may help. Since the important filariasis caused by *Wuchereria bancrofti* cannot be given to animals, patients with onchocerciasis provide a research reservoir for the easier study of the general aspects of filarial infection in man.

These research studies will help also in the search for an effective therapy for these diseases. At present the treatment of onchodermatitis is the removal of palpable onchocercomas, the symptomatic therapy of the cutaneous lesions especially as regards pruritus and the general treatment of the patient as concerns avitaminosis, intestinal parasitism and the like. Experiments have been started with topical applications to determine penetration and absorption in the skin. Perhaps there may be some effect on microfilariae. The heavy fibrous coating of the onchocercoma seems to preclude local penetration effects on adult worms. Moreover, this location of the nodules is too deep for penetration and absorption from the cutaneous surface. The local materials which we have started to use, on the advice of Kehoe<sup>4</sup> and Deichmann,<sup>4</sup> include pentachlorophenols, pentachlorophenates, ethylene dibromide and DDT. Since the microfilariae migrate in the pars papillaris, it is hoped that at least these chemicals may be able to prevent microfilariae from reaching the eyes. This could be done through hindrance to progress in superficial tissues about the eyes, by changes in "tissue reaction." Such changes in tissue would be preferred to direct toxic action on the parasite, since this reaction may serve to produce a local inflammatory change which the dead microfilariae (alone?) are supposed to cause, a type of "therapeutic paradox." Much more work is needed in the possibility of immunotherapy as a practical aid, since this phase is so little understood at present.

#### CONCLUSION

The forms of dermatitis seen in patients with onchocerciasis at the Centro Médico in Huixtla, Chiapas, Mexico, and gathered from the records there indicate that *mal de morado* (*dermatosis onchocerosa pigmentada*) acute and chronic edemas, lichenifications and eczematoid reactions are some of the types of onchodermatitis. The edema reactions show some slight general resemblance to the edema of filariasis caused by *Wuchereria bancrofti*. There is difficulty in interpreting these cutaneous reactions in a critical fashion because of the lack of

knowledge concerning some basic mechanisms of the infection due to *Onchocerca volvulus* in man, such as the immunobiology, and the evaluation of such important associated conditions as avitaminosis, intestinal parasitism, sensitivity phenomena and other mechanisms of the reaction to the bite of a simuliid and finally the lack of specific therapy. The treatment of onchodermatitis is essentially the treatment of the patient's onchocerciasis and the local symptomatic therapy of the type of dermatitis produced. It is emphasized that onchocerciasis provides a readily available clinical group for the study of the general principles of filarial infection in man.

## LEMON GRASS OIL

A Primary Irritant and Sensitizing Agent

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NEW YORK

**I**N a previous communication,<sup>1</sup> I reported an outbreak of an acute eruption resembling poison ivy dermatitis in approximately 30 men, presumably due to lemon grass oil. Eight of the affected persons were observed by me.

These men had worked as machinists, carpenters and riggers on a boat which had recently arrived from India. Part of the cargo consisted of tanks of lemon grass oil, some of which had spilled and evidently had found its way to different parts of the boat. The eruption appeared six to eighteen days after the men had worked on the boat.

The diagnosis was based on the history and clinical appearance of the eruption and on a strongly positive reaction (erythematovesicular and vesiculobullous) to a patch test with pine wood soiled with lemon grass oil. I was unable to obtain a sample of lemon grass oil for use in patch tests.

After the acceptance of the manuscript for publication, Dr B A Bourne, Director of Research, United States Sugar Corporation, supplied me with a sample of lemon grass oil from the Florida Everglades containing approximately 75 per cent of citral, a diolefinic aldehyde and a common constituent of essential oils. The usual citral content of lemon grass oil is 70 to 80 per cent.<sup>2</sup>

An accompanying note read in part as follows: "For your information we would say that in our experience we have found some persons to be rather sensitive to the action of lemon grass oil on their skin, while others showed no reaction although their hands were exposed directly to it for weeks at a time. Undoubtedly the irritating

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1 Mendelson, H V. Dermatitis from Lemon Grass Oil (*Cymbopogon Citratus* or *Andropogon Citratus*), *Arch Dermat & Syph* **50** 34 (July) 1944.

2 Cohen, J B. Organic Chemistry for Advanced Students, New York Longmans, Green & Co, 1907.

agent is the aldehyde citral, and it would appear that its reaction depends largely on the individual "

After the publication of my report, Dr M B Luthy, of Givaudan-Delawanna, Inc, sent me samples of lemon grass oil from two different sources one from India, with a citral content of 75 per cent, the other from Guatemala, with a citral content of 76.2 per cent. A note from him contained the following comments "We have used large quantities of lemon grass oil in our factory for about twenty years. We have never taken any special precautions but have not encountered cases of dermatitis due to the handling of this oil. We would think that your statement 'Lemon grass oil is a primary irritant and/or strong sensitizing agent' needs further checking."

Through the kindness of Mr Charles A Buckie, Van Ameringen-Haebler, Inc, supplied me with samples of three different ionones alpha ionone, methyl ionone and extra pure ionone. These are complex chemical isolates from lemon grass oil, in which the aldehyde citral is converted to a ketone. Because of their high aromatic qualities, they are extensively used in perfumes, toilet waters, lipsticks and other cosmetics.

#### INVESTIGATION

Patch tests with the three lemon grass oils and the three ionones were performed on 20 patients with different dermatoses, including acne, dermatitis venenata, dermatophytosis, eczema, folliculitis, impetigo and others. The lemon grass oils were employed in three dilutions full strength, 1:10 and 1:100. The dilutions were made with olive oil. The ionones were used undiluted.

Fifteen patients received twelve tests, five received only nine tests. Altogether two hundred and twenty-eight tests were applied. Patch tests with the undiluted lemon grass oils were removed after twenty-four hours, those with the different dilutions and with the ionones were left on for forty-eight hours. Reactions were read when the patches were removed, and thereafter the areas were examined every two or three days for several weeks.

The table shows that in general the different lemon grass oils elicited similar reactions. The undiluted lemon grass oils elicited 3+ and 4+ reactions in all persons tested. The reactions were mainly vesiculobullous, and most of them persisted for eighteen days. In one instance (case 2) evidence of the reactions was present on the forty-fifth day in the form of brownish pigmentation with slight scaling. In another case (case 3), the reactions disappeared on the twentieth day leaving vitiliginous areas which were present four months later, when the person was last seen.

In 2 cases (cases 3 and 19) all the oils elicited 1+ reactions in dilutions of 1:10, an incidence of 10 per cent, in 1 other person, only the Florida oil elicited a 1+ reaction in a similar dilution, an incidence



# Detailed Tabulation of Total Number of Patients Tested and Reactions

Patient	Initials	Age, Years	Sex	Race	Diagnosis	Hours	Material	Reaction	Material	Reaction	Material	Reaction	Comment
1	M G	40	F	N	Urticaria	24	F	+++	G	+++	I	+++	After 15 days no evidence of reaction
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
2	J A	14	F	W	Acne	24	F	++++	G	++++	I	++++	Slight evidence of reaction on the 45th day in form of brownish pigmentations and slight scaling
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
3	B D	16	F	W	Acne	24	F	++++	G	++++	I	++++	4+ reactions persisted for 20 days, leaving vitiliginous areas present 4 months later, 1+ reactions cleared within 1 week
						48	10	+	10	+	10	+	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
4	M D	43	F	W	Dermatitis venenata	24	F	+++	G	++++	I	+++	2+ delayed reaction in all sites of tests with 1:10 dilutions 6 days after patches removed
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
5	S H	63	M	W	Poison ivy dermatitis	24	F	+++	G	+++	I	+++	
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
6	J A	25	F	N	Syphilis	24	F	++++	G	++++	I	++++	Reaction persisted for 15 days
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
7	A S	31	F	N	Syphilis	24	F	++++	G	++++	I	++++	
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
8	S J	36	F	N	Pityriasis versicolor	24	F	+++	G	+++	I	+++	No evidence of reaction at end of 20 days
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
9	L R	34	F	N	Chronic eczema	24	F	++++	G	+++	I	+++	
						48	10	+	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
10	F L	12	F	N	Impetigo	24	F	—	G	—	I	—	
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
11	H C	24	F	N	Folliculitis	24	F	+++	G	+++	I	+++	Evidence of reactions present 12 days
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
12	H C	33	F	N	Syphilis	24	F	—	G	—	I	—	
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
13	J F	36	M	W	Dermatitis venenata	24	F	++++	G	+++	I	+++	
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
14	J S	54	M	W	Dermatitis venenata	24	F	++++	G	++++	I	++++	4+ reactions persisted for 21 days, doubtful reaction to I e p disappeared within 48 hours
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	+	
15	W F	53	M	W	Chronic eczema	24	F	++++	G	++++	I	++++	Severe reaction from adhesive
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
16	S P	69	M	W	Dermatitis venenata	24	F	+++	G	+++	I	+++	
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
17	P M	64	M	W	Chronic eczema	24	F	—	G	—	I	—	Doubtful reaction to I e p disappeared within 48 hours
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	+	
18	J C	70	M	W	Dermatitis venenata	24	F	—	G	—	I	—	Severe reaction from adhesive
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
19	E N	64	M	W	Chronic eczema	24	F	++++	G	++++	I	++++	4+ reactions persisted 18 days 1+ reactions disappeared within 1 week
						48	10	+	10	+	10	+	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	
20	J H	40	M	W	Dermato phytosis	24	F	—	G	—	I	—	Severe reaction from adhesive
						48	10	—	10	—	10	—	
						48	100	—	100	—	100	—	
						48	I a	—	I m	—	I e p	—	

Legend F = Florida lemon grass oil undiluted G = Guatemala lemon grass oil undiluted, I = India lemon grass oil undiluted 10 = dilution 1:10 100 = dilution 1:100 I a = ionone alpha undiluted I m = ionone methyl undiluted, I e p = ionone extra pure undiluted

of 15 per cent. These reactions were chiefly erythematous and persisted for five days.

In 1 case (case 4) there was a delayed 2+ reaction in all sites with the 1:10 dilutions, an incidence of 5 per cent. The reaction appeared six days after the patches were removed, it was erythematovesicular and healed within ten days, with desquamation.

No positive reactions were obtained by any of the tests with oils in dilutions of 1:100.

The three ionones elicited negative reactions in all subjects, except for a doubtful reaction in 2 persons (cases 14 and 17). These reactions were erythematous and disappeared within forty-eight hours.

#### COMMENT

The strongly positive reactions to undiluted lemon grass oil from three different sources in every one of 15 persons tested indicate that this oil from any source with a citral content of 75 per cent or over is a primary irritant. Whether the citral or some other substance is the irritating agent, this study does not reveal. Bourne<sup>3</sup> is of the opinion that this aldehyde is the specific irritant.

The high incidence of 1 plus reactions (10 per cent) to oils obtained from Guatemala and India in dilutions of 1:10 and 1 plus reactions (15 per cent) to the Florida oil in a similar dilution suggests probable primary irritation. On the other hand, the wide use which these oils and their products enjoy affords ample opportunity for adequate contact and sensitization, and these reactions may be expressions of specific sensitivity. In any event, it seems reasonable to assume that, because of one mechanism or another, these oils may "irritate" certain persons even in dilutions of 1:10.

The 2 plus delayed reactions on the sixth day to all the oils in a dilution of 1:10 in 1 case are most interesting. These undoubtedly represent manifestations of induced epidermal sensitivity—"spontaneous flare-up" of Sulzberger<sup>4</sup>. Evidence for this assumption is not only the development of typical eczematous reactions at the test sites six to eight days after initial contact with the oils (adequate sensitization period) but the fact that when the patient was retested three weeks later with the same oils in 1:10 dilutions 1 plus to 2 plus reactions (erythema and vesiculation) were noted at all sites immediately on removal of the forty-eight hour test patches. From this it may be

<sup>3</sup> Bourne. Personal communication to the author.

<sup>4</sup> Sulzberger, M. B. *Dermatologic Allergy*. Springfield, Ill., Charles C. Thomas, Publisher, 1940.

inferred that lemon grass oil in low dilutions possesses allergenic qualities and is a competent sensitizing agent

The ionones which were investigated were, as a class, found nonirritating and in all likelihood nonsensitizing. To determine the significance of the doubtful reactions to the extra pure ionone in the 2 test subjects would require further study

I am fully aware of the small number of persons tested and the conservatism which must be employed in evaluating results. I feel, however, that the goodly number of patch tests applied (altogether 228) and the careful attention given to this investigation justify my interpretations

#### CONCLUSIONS

1 Lemon grass oil from any source, with a citral content of 75 per cent or over, is a primary irritant, in a dilution of 1:10 it is a sensitizing agent

2 Alpha, methyl and extra pure ionones are nonirritating and, in all likelihood nonsensitizing

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## ERYTHEMA EXUDATIVUM MULTIFORME

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**E**RYTHEMA exudativum multiforme is an acute infection which manifests itself by a systemic reaction and an eruption which is polymorphous in character. The lesions are often symmetrically distributed over the upper and lower extremities, as well as on the chest and face and may be accompanied by involvement of the mucous membranes. The disease is often recurrent.

Hebra<sup>1</sup> (1866) first described this disease, which consequently sometimes bears his name. He considered it a systemic and not a local disturbance, recognizing no causation. Fuchs<sup>2</sup> (1876) first described the ocular complications of this disease. Geike and Kain<sup>3</sup> (1892), de Molènes-Mahon<sup>4</sup> (1884) and von Düring<sup>5</sup> (1896) also recorded adequate descriptions. Kaposi<sup>6</sup> (1893) noted the variegated form of the lesions, which ranged from vesicular to iris in type. Further contributions to the literature were made by Hanke,<sup>7</sup> Crocker<sup>8</sup> and Mracek.<sup>9</sup>

In 1913 H. Barkan<sup>10</sup> reported an interesting case which he had observed in Fuchs's Clinic. The disease progressed until the patient completely lost vision following corneal ulceration. In 1921 Hartley<sup>11</sup>

1 Hebra, F. Diseases of the Skin, translated and edited by C. H. Fagge, London, New Sydenham Society, 1866, vol. 1.

2 Fuchs, E. Herpes Iris Conjunctivae Beobachtet, Klin. Monatsbl. f. Augenh. **14** 333, 1876.

3 Gerke, O. and Kain, E. Ein Fall von Croup der Bindehaut der Mund- und Rachenschleimhaut, Arch. f. Augenh. **24** 305, 1892.

4 de Molènes-Mahon, P. Contribution à l'étude des maladies infectieuses, Thesis, Paris, no. 61, 1884.

5 von Düring, E. Beitrag zur Lehre von den polymorphen Erythemen, Arch. f. Dermat. u. Syph. **35** 211, 1896.

6 Kaposi, M. Pathologie und Therapie der Hautkrankheiten, ed. 4, Vienna, Urban & Schwarzenberg, 1893.

7 Hanke, V. Der Herpes iris des Auges, Arch. f. Ophth. **52** 263, 1901.

8 Crocker, H. R. Diseases of Skin, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1903.

9 Mracek, F. Handbuch der Hautkrankheiten, Vienna, Alfred Holder, 1902, vol. 1, p. 540.

10 Barkan, H. Herpes Iris of the Conjunctiva, Arch. Ophth. **42** 236, 1913.

11 Hartley, C. C. Ueber die Kombination der Conjunctivitis et Stomatitis pseudomembranacea und ihr Verhältnis zum Erythema multiforme und Pemphigus, Klin. Monatsbl. f. Augenh. **67** 23, 1921.

pointed out the similarity of erythema exudativum multiforme to pemphigus and showed that both diseases produced an essential conjunctival shrinkage. In 1922 Stevens and Johnson<sup>12</sup> described a "New Eruptive Fever Associated with Stomatitis and Ophthalmia" usually terminating with irreparable damage to the eye, subsequently referred to as Stevens-Johnson Disease. Wheeler<sup>13</sup> (1930) described a case in which there was complete loss of vision in both eyes. In 1931 Bailey<sup>14</sup> published a comprehensive review of the literature, in which he described the corneal and conjunctival lesions in detail. Among other things he pointed out that the disease was analogous to an acute infection in its onset and its various sequelae, that there were inflammatory changes in the cornea and conjunctiva which might lead to impairment or loss of vision, that there was intense pseudomembranous inflammation of the buccal structures, lips, upper respiratory tract, bronchi and sometimes the vagina, that there was widespread polymorphous eruption of the skin, that there was a widely varying leukocyte count, and that the course may be protracted, extending over weeks, with a favorable prognosis except for ocular changes. Ginandes<sup>15</sup> (1935) emphasized the presence of increased monocytes in the blood, in this disease. He also cultivated *Staphylococcus aureus* from the conjunctiva and from the cutaneous vesicles. Elson<sup>16</sup> (1937) described a treatment for erythema exudativum multiforme assuming that it was a disease caused by an intrinsic allergic toxin. He stated that there are two types of erythema exudativum multiforme, one being of short duration and the other of long duration. Bregman<sup>17</sup> reported a case of erythema multiforme which he had treated with sulfanilamide apparently with good results. Edgar and Syverton<sup>18</sup> in 1938 described 2 cases of erythema exudativum multiforme associated with ophthalmia and stomatitis. A biopsy of the skin was performed which showed

12 Stevens, A. M., and Johnson, F. C. New Eruptive Fever Associated with Stomatitis and Ophthalmia, *Am J Dis Child* **24** 526 (Dec) 1922

13 Wheeler, J. Destructive Purulent Ophthalmia Accompanying Eruptive Fever and Stomatitis, *Am J Ophth* **13** 508, 1930

14 Bailey, J. H. Lesions of the Cornea and Conjunctiva in Erythema Exudativum Multiforme (Hebra). Report of Three Cases with Grave Ocular Sequelae, *Arch Ophth* **6** 362 (Sept) 1931

15 Ginandes, G. J. Eruptive Fever with Stomatitis and Ophthalmia. Atypical Erythema Exudativum Multiforme (Stevens-Johnson), *Am J Dis Child* **49** 1148 (May) 1935

16 Elson, L. N. Treatment of Erythema Multiforme Exudativum, *Urol & Cutan Rev* **41** 812, 1937

17 Bregman, A. Treatment of Erythema Multiforme Exudativum with Sulfanilamide. Report of a Case, *Arch Dermat & Syph* **38** 623 (Oct) 1938

18 Edgar, J., and Syverton, J. T. Erythema Exudativum Multiforme with Ophthalmia and Stomatitis. Report of Two Cases in Children with Certain Observations on Histopathology and Animal Inoculation, *J Pediat* **12** 151 1938

the characteristic pathologic lesion. An attempt to demonstrate inclusion bodies was unsuccessful. Keil<sup>19</sup> (1940) thoroughly reviewed the disease, stating the belief that it was a clinical entity associated with certain specific systemic features. That same year Ester Gronblad<sup>20</sup> pointed out the relationship of erythema exudativum multiforme of ocular type to other conjunctival diseases producing essential shrinkage. She suggested a toxic cause precipitating an attack, usually in the form of some internal medication. Givner and Ageloff<sup>21</sup> reported 3 cases called "Stevens-Johnson Disease" with complete visual recovery. They corroborated reports of benefits derived from the sulfonamide drugs. They also emphasized the presence of *Staph aureus* recovered from the conjunctiva and vesicles. However, they failed to grow any virus on chick embryo. They, again, emphasized the increased monocyte count. Givner and Ageloff mentioned the use of cod liver oil locally along with the liberal use of vitamin B and C, but did not state whether the whole vitamin B complex was used or only fractional constituents. No comment was made concerning the nature of the diet nor was there mentioned evidence of avitaminosis systemically in these persons.

#### REPORT OF CASES

CASE 1—A 28 year old colored man was admitted to the hospital on Jan 10, 1942, with the chief complaint of sore throat and cough, of one week's duration. The only significant physical findings were an injected pharynx and many sibilant and sonorous rales throughout the chest. A diagnosis of acute tracheobronchitis was made and treatment instituted accordingly.

The following day his temperature rose to 104 F and excessive cough developed. There was dulness over both lower lobes of the lungs associated with many crepitant rales, most evident over the right lower lobe. His white blood count was 12,750 per cubic millimeter with 88 per cent polymorphonuclear cells, 7 per cent lymphocytes and 5 per cent monocytes. From these findings a diagnosis of pneumonitis at both bases was made. The patient was given sulfathiazole with an initial dose of 4 Gm, followed by 1 Gm every four hours. His temperature remained between 103 and 104 F, the pulse rate 128 per minute and the respiration 28 per minute. On February 14 a few hemorrhagic blebs developed on the chest and extensor surface of the forearms. Sulfathiazole was discontinued in view of a possible reaction to the drug. On February 15 many vesicular lesions appeared on the face, ears and hands. There was decided conjunctivitis. The nose was somewhat swollen, the lips were fissured and bleeding, the pharynx was injected, many hemorrhagic areas were present on the gums and palate, and small ulcerative areas were present over the entire buccal mucous membrane. Three

19 Keil, H. Erythema Exudativum Multiforme (Hebra). A Clinical Entity Associated with Systemic Features, *Ann Int Med* **14** 449, 1940.

20 Gronblad, E. Ocular Associations of Diseases of the Skin, in Ridley, F., and Sorsby, A. *Modern Trends in Ophthalmology*, London, Butterworth & Co., Ltd, 1940.

21 Givner, I., and Ageloff, H. Stevens-Johnson Disease with Complete Visual Recovery, *New York State J Med* **41** 1762, 1941.

consecutive smears of the oropharynx for Vincent's spirillum failed to disclose the presence of that organism. A diagnosis of erythema multiforme with typical iris, bullous and mucous membrane lesions was made at this time, confirmed by the dermatologist.

Further inquiry was made into the previous personal history of the patient. In April 1938, he was confined to bed for several days with a sore throat, a mucocutaneous eruption and a severe cough. The patient was told that he had small-pox, for which he was quarantined. Inquiry was also made as to his diet, and it was learned that his food consisted chiefly of bread, milk and corn and rarely meat, fruits and vegetables.

As the similarity of the patient's oral lesions to those seen in pellagra, was recognized, he was given nicotinamide in doses of 100 mg tablets four times daily.

The eyes disclosed a definite sparseness of the cilia of both lids of both eyes. The few lashes that were present were irregular in size and varied as regards direction of growth. A fair amount of secretion was present in the cul-de-sac and on the eyelashes. The bulbar conjunctiva was decidedly injected, the palpebral moderately so. The media were clear and the fundi were normal. The ocular picture suggested acute conjunctivitis associated with an upper respiratory infection. Warm boric acid compresses three times a day and a 20 per cent dilution of mild protein silver (Argyrol), 2 drops three times a day, were suggested.

When the patient was examined forty-eight hours later the eyelids were moderately edematous and the skin of the region of the entire lower lid was excoriated and had fallen off in patchy areas, producing a "geographic" appearance of bleeding red islands punched out prominently in a semicircular edematous lower lid. There were many small, bleeding angry-looking irregular areas. The margin of the lids was pulled away from the globe because of the weight of the fluid and because bilateral ectropion appeared to be developing. The conjunctivas, both bulbar and palpebral, were much more involved than on the previous examination, the cornea, however, was absolutely clear, and no involvement of the media or fundus was observed. There was a herpetic lesion on the lid and about the external nares, extending down to the lips. When viewed "in toto" the picture suggested that a drug had been used in the eye to which the patient was sensitive, and that there had been an extension of this sensitizing process through the nasolacrimal duct into the nose and into the nasopharynx, external nares and lips. However, the appearance of a specific cutaneous eruption at this time called to mind the presence of a generalized disturbance of the mucous membranes. The mild protein silver was discontinued, and the patient was given a 3 per cent dilution of homatropine hydrochloride solution, 1 drop in each eye three times a day, together with hot boric acid compresses and boric acid ointment. The patient was watched carefully for formation of adhesions of the conjunctivas and for corneal involvement.

From the onset photophobia and lacrimation were predominant symptoms. At no time was there any follicle formation or areas of localized hemorrhage or necrosis.

The appearance of the lids did not vary perceptibly in the first week, although the possible development of adhesion and ectropion seemed to suggest itself. The original bleeding lesions of the lid were well encrusted within five days after the onset. The eyelids, which previously had drooped considerably, began to be opened more widely and the tendency toward ectropion rapidly disappeared.

The patient's temperature fell to normal on the seventh day of his hospital stay and remained normal thereafter. On February 23, he appeared to be greatly improved. Circinate lesions were observed on the face, legs, forearms, chest and



hands. The scrotal involvement was unchanged. There was no adenopathy. The eyes showed great improvement. The patient was able to open his mouth without causing blood to ooze. The lips were smooth. The lesions on the tongue and mucous membranes seemed to be regressing. The patient's appetite continued to improve as his cough became less disturbing. On March 4, the lesions in the mouth, involvement of the conjunctiva and scrotal edema had completely subsided. The lesions on the hands, chest, feet and face showed signs of desquamation. There were only a few sibilant and sonorous rales in the right lower thoracic region.

The patient was maintained on nicotinamide from February 14 until the time of his discharge, receiving 400 mg by mouth daily.

CASE 2—The patient was a 22 year old Indian whose chief complaint was sore mouth, throat and tongue and a moderately severe cough. The symptoms started three days before his admission to the hospital on May 10, 1942. At the onset the patient also suffered from photophobia and lacrimation of both eyes, difficulty in swallowing and inability to open his mouth widely. The physical examination disclosed a well built adult man apparently uncomfortable, being unable to talk, swallow or open his mouth. The eyes appeared to be rather sensitive to light. A sticky secretion was visible at the margins and inner canthus of each eyelid. The inner surface of each lower lid was red and coated by a thin sanguineous layer. There was no follicle formation but a "beefy" congestive appearance. When the upper lids were everted a horizontal white band, vaguely resembling Arlt's line seen in trachoma, appeared to stand out in striking contrast to the red conjunctival background. The bulbar portion of the conjunctiva was mildly injected. The slit lamp examination added no new observations.

On forced opening of the mouth, many ulcerated and hemorrhagic areas were seen in various parts of the mucous membrane, including the buccal, lingual, pharyngeal and palatine surfaces. These areas were spongy, exudative and hemorrhagic. With a new technic of examination in which the slit lamp microscope and slit lamp beam of light were used, it was possible to examine the mucous membrane of the gums and tongue. These structures showed some particularly interesting and characteristic features. About 1 mm from the edge of the gums, just before that structure reaches the tooth, the tissue appeared suddenly to become elevated. The mucous membrane was hyperemic due to the great increase in number of capillary loops which stood out like little red pinheads. Some of these loops could be seen running along for a short distance almost to the edge of the gum. The small lingual folds located on the under surface of the tongue just lateral to the large veins particularly illustrated the increased hyperemia manifested by excessive capillary loop formation in these folds.

In the nose there were many ulcerative and bleeding lesions of the mucous membrane. Excoriations extended onto the cutaneous area of the upper lips, which were created by a serum-like and hemorrhagic coating. Typical iris lesions were present on the skin of the face, ears, forearms, chest and feet. In forty-eight hours these elevations, which became bullous, ruptured, producing ulcerative surfaces. The patient was referred to the dental department, where a diagnosis of Vincent's angina was made. At the time he was referred to the eye department he had been receiving the routine local therapy, consisting of saline and perborate mouth washes, of gentian violet medicinal applications and local massage therapy. On recognition of the disease as erythema exudativum multiforme, it was suggested that all local therapy be discontinued, and that the patient be given only nicotinic acid orally (400 mg daily) for three days and a diet adequately reenforced with vitamins if he was able to consume such a diet. The blood count showed 10,400

white blood cells, with 85 per cent polymorphonuclears, 6 per cent monocytes and 9 per cent lymphocytes

When the patient was again seen after forty-eight hours the temperature was 98.6 F. He was able to open his mouth widely so that the rapidly healing ulcers could be seen. There was little residue of conjunctival, buccal, nasal and gingival inflammatory manifestations. His appetite had returned, and his mental attitude showed a striking "pick up." There was no soreness of tongue, throat or gums. The microscopic capillary loops of gums and tongue were much less prominent. The cutaneous lesions, although still present, were no longer in an acute phase. In another forty-eight hours under the same therapy the patient felt completely well, and all the previously reported lesions were well on the road to complete disappearance.

CASE 3—A 23 year old man had been treated at the dental clinic for one week because of an infection of the mouth which was believed to be Vincent's angina. There were many lesions of the mucous membrane of the mouth, pharynx, tongue and throat, containing a small ulcerated central zone and a surrounding area of hyperemia. The edge of the gum margin showed an area of elevation and increased vessel loop formation, much like that described in case 2. The results of the slit lamp study in this case conformed in all details to that of the second case except that they were much less severe. The lingual folds of the tongue showed a condition identical with that described in the second case. Three days after treatment had been instituted at the dental clinic a cutaneous eruption appeared on the face, extensor surface of the forearms, the chest and the thighs. The patient was referred to the dermatologic clinic at this time, and a diagnosis of erythema multiforme was made. Because of the patient's inability to open his mouth and swallow food, he was admitted to the hospital. On the initial examination it was found that the patient had a temperature of 101.4 F., and that the lesions of the mouth and skin had progressed. Although the patient had no complaints referable to his eyes, examination disclosed a definite congestion of the conjunctiva with some secretion occupying the inferior cul-de-sac of each eye. The congestion primarily involved the palpebral rather than the bulbar conjunctivas and was of rather mild character. There was no definite sensitivity to light, for the cornea was uninvolved. In the next three days the patient's eye became somewhat more reddened and the lid margins became encrusted from the ocular secretions.

Immediately on entrance into the hospital, the patient was given nicotinic acid orally (400 mg. daily). Intake of liquids was increased, the aim being to give him fluids rich in vitamins and at the same time not difficult to swallow. After four days there was decided improvement in the patient's general condition. The lesions of the oral mucous membrane had almost entirely disappeared, and the cutaneous lesions were well on the way to complete healing. The microscopic examination of the gingival and lingual tissues viewed through the slit lamp showed a decrease in the number of capillary loops and a definite reduction in the amount of swelling in the area near the teeth. The patient was discharged from the hospital at the end of six days with the lesions of the mucous membrane apparently cured and with almost complete disappearance of the disturbance of the skin.

In this case no other medication was used except a saline gargle for forty-eight hours, to see what effect the use of nicotinic acid alone would have on the mucocutaneous lesions. At the end of this period the temperature was normal, the mouth was in no way uncomfortable and the cutaneous lesions were beginning to respond. The blisters of the skin were already dry.

## COMMENT

The treatment of erythema exudativum multiforme in the past has been varied and largely empiric. In reviewing the literature of the past fifteen years it becomes evident that an extremely great number of drugs have been employed, each the particular favorite of the author. The majority of remedies used were largely of supportive nature. With the advent of chemotherapy, the sulfonamide drugs may act like an allergic toxin in precipitating this symptom complex, and so chemotherapy has not played any major part in the new knowledge of therapy for erythema exudativum multiforme. Kiel, however, stresses its prophylactic benefits in warding off hypostatic pneumonia in the elderly patient suffering from this disease.

The newest and least exploited form of therapy introduces use of vitamins for this generalized mucocutaneous disease. For the most part the therapy has been given without specific or rational indication except as a general supportive agent. Because of this varied therapy, and, as we have previously mentioned, because of the similarity of some of the lesions of the mucous membranes in erythema exudativum multiforme to those seen in avitaminosis B, the use of large doses of nicotinic acid immediately suggested itself as a rational therapeutic procedure. For this reason the patients were given 100 mg. of the aforementioned vitamin four times a day. As supportive measures they received liquid nourishment in large quantities. Within an extremely short time a striking improvement was noted, especially as manifested by the lesions of the mucous membranes. The patients soon showed an improvement in their mental condition, changing rapidly from the semilethargic state to one of actual alertness. Anorexia was rapidly replaced by ravenous appetite and an interest in the surroundings developed along with a desire to get out of bed. The cutaneous lesions showed rapid regression, and interestingly enough the new crop of lesions left no visible sequelae. In each eye symptoms abated entirely within a few days, except for the presence of scarlike formation of the upper lids. When the lids were averted in cases 1 and 2 a small semilunar scar running the length of the lid was seen. The normal parallel rows of the meibomian glands were absent. The lids presented the essential shrinkage of the conjunctiva which is the important clinical finding in this modified ocular picture. In case 1, three weeks after the onset of the illness a section of tissue was removed from the right upper lid for purposes of pathologic study. This section was taken through the entire thickness of the lid except the skin and was selected through an area of visible scar formation on the inner surface of the lid. The report on the pathologic section follows.

The specimen consisted of a piece of opaque, fibrous tissue measuring 6 by 2 by 2 mm. There was partial desquamation of the conjunctival epithelium. The subepithelial tissues were edematous and infiltrated predominantly by lymphocytes. Occasional eosinophils were seen. Capillary proliferation was present. There were a slight chronic inflammatory cell infiltration of the tarsal plate and some dilatation of the meibomian glands.

The diagnosis was chronic, severe, nonspecific inflammatory reaction.

Keining and Oldach<sup>22</sup> have shown in a series of 24 cases of characteristic erythema exudativum multiforme that the use of nicotinamide is a decided improvement in our dermatologic armamentarium. After two and sometimes after three intramuscular injections of nicotinamide, decided regression of the symptoms was noted both systemically and locally. Rarely did it take as many as six or seven injections. Ampules containing 1 cc. were used, 3 cc. being given at each dose.<sup>23</sup> The authors also advocated the continuance of the drug long after subsidence of symptoms so that no recrudescence would occur.

#### SUMMARY AND CONCLUSIONS

1 Erythema exudativum multiforme is a single clinical entity, which may involve the skin and any of the mucous membranes and should not be separated into symptom complexes.

2 At the onset a difficult diagnostic problem may present itself, because of the resemblance of this disease to other diseases.

3 Erythema multiforme evidently has some relationship to avitaminosis B, especially to lack of nicotinamide.

4 Nicotinamide should be given in massive doses to secure the best results. The symptoms of adequate dosage are usually manifested by a flushing of the skin, a feeling of warmth, slight dizziness and a sense of alertness.

5 In the mild conjunctival type of ocular involvement there is present an essential shrinkage of the conjunctiva. Recurrences are common unless the high vitamin concentration is continued even after recovery.

6 In cases in which the patient is not able to take the medication orally, nicotinamide should be given intravenously or intramuscularly in similar dosage.

7 The importance of slit lamp examination and nature of the lesions of the mucous membrane in this condition is stressed.

<sup>22</sup> Keining, E., and Oldach, F. A. Behandlungsergebnisse mit Nikotinsäureamid bei multiformen Erythemen, *Dermat. Wchnschr.* **112**: 285, 1941.

<sup>23</sup> Merck's preparation was used.

## ERYTHEMA STREPTOGENES

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AND

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STREPTOCOCCIC dermatoses are numerous and have been described by various investigators under various names. The majority of the streptococcic dermatoses are characterized by abundant exudation of serum during some phase of the disease (impetigo, streptococcic intertrigo, perleche, ecthyma, streptococcic dermatitis and others)<sup>1</sup>. Dry scaling without exudation may affect the auditory canal<sup>2</sup>. Sutton and Sutton<sup>3</sup> in their textbook briefly mentioned the chronic dry type of streptococcus infection which is seen on the face in the form of furfuraceous patches of circular or irregular outline practically asymptomatic except for the branny desquamation. This eruption apparently parallels the pityriasis simplex of the face, called by the French authors *dartres volantes*. These are seen chiefly in children and in former times were regarded as evidence of a strumous diathesis. The lesions are circular or oval, superficial, well defined and covered with fine branny scales. Impetigo pityrioides<sup>4</sup> is occasionally seen toward the end of an attack of ordinary impetigo, and one may see in the same patient all stages of the disease, from the crusted oozing lesions to the dry scaly patches which resemble pityriasis simplex.

For several years a dry, chronic dermatosis has been observed among the Negro population in the southern states. Patients with this dermatosis are seen frequently in the dermatologic clinics of the Negro division of Grady Hospital. The dermatosis is commonly referred to as "erythema streptogenes". A survey of the literature shows no reference to a disease under this name.

From the Department of Dermatology, Grady Hospital (Negro division), Emory University School of Medicine

1 (a) Chipman, E D. Streptococcic Dermatoses, Arch Dermat & Syph (Oct) 1921. (b) Kinnear, J. Brit J Dermat 48 173, 1936.

2 Mitchell, J H. Streptococcic Dermatoses of Ears, J A M A 108 361 (Jan 30) 1937.

3 Sutton, R L, and Sutton, R L, Jr. Diseases of the Skin, ed 10 St Louis, C V Mosby Company, 1932, p 902.

4 Barber, H W. Lancet 2 35, 1935.

## CLINICAL COURSE

Erythema streptogenes appears in young children, both Negro and white, but more frequently in Negro children. Adults may be affected. The primary lesion appears as a macule, or a mild form of dermatitis may be present. The dermatitis is fairly well circumscribed and asymptomatic in most cases. Some children complain of itching and burning which is not severe. The areas which are usually affected are the cheeks, the forehead or other parts of the face. The eruption rarely appears on other parts of the body. The redness usually subsides within one to two weeks, and the areas involved become scaly and wrinkled and partial depigmentation slowly appears (fig 1). As the depigmentation becomes more pronounced, the scaling and wrinkling become lessened.



Fig 1—Erythema streptogenes. Lesions around mouth show slight erythema, fine scaling and early partial depigmentation. Duration is two and one-half months. Lesion on forehead shows no erythema. The depigmentation is more advanced. Duration is three and one-half months. Cultures from both sites yielded the hemolytic streptococcus.

Within two to three months only a circumscribed patch of partial depigmentation is present, which is slightly scaly (fig 2). In early lesions the borders are ill defined, but in the later stages these are more pronounced. The patch of partial depigmentation remains stationary and unchanged indefinitely (fig 3). Peripheral spread is unlikely once the erythema has subsided. The depigmented areas resemble those of vitiligo, however, the depigmentation of vitiligo is more pronounced and sharply defined. The borders of the lesions of vitiligo usually show some hyperpigmentation. The lesions of erythema streptogenes remain smooth.

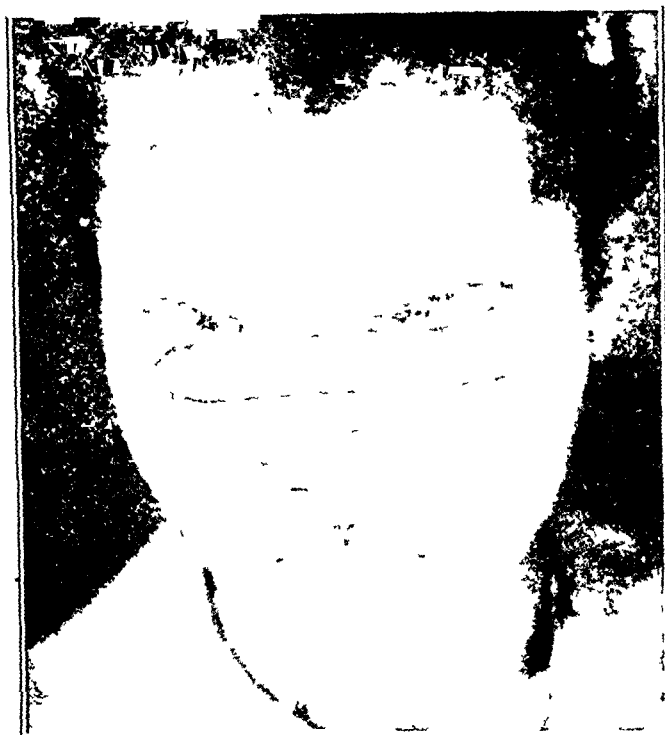


Fig 2—Erythema streptogenes. Small areas of partial depigmentation fused to give the mottled appearance. The eruption is beginning to clear under treatment.

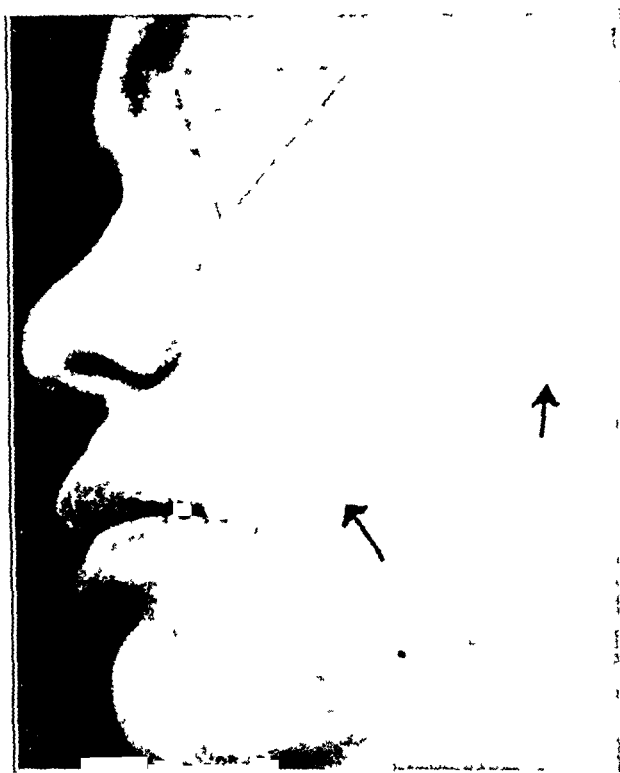


Fig 3—Small areas of partial depigmentation (1 to 5 mm). The size of the depigmented patches has not changed for the past eight months. The culture was positive for the hemolytic streptococcus. The eruption cleared with treatment.



or else a fine branny scale is present, which is best seen with a magnifying glass. The depigmented patches may persist for several years (fig 4). Rarely, they subside without treatment after several months' duration. The general health of the patient is not affected.

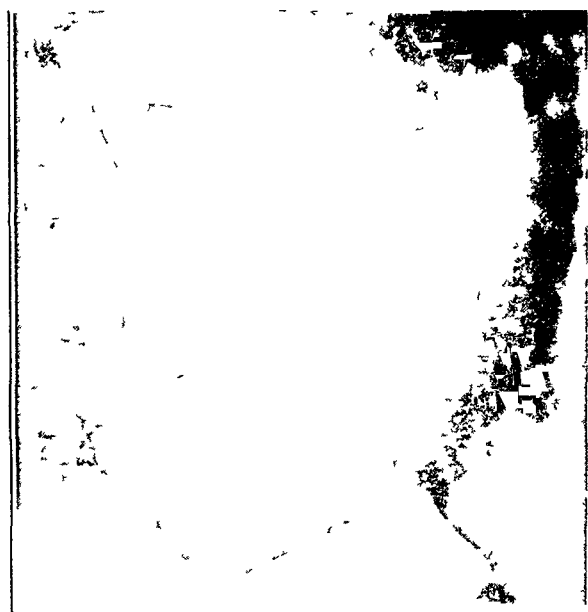


Fig 4—A single depigmented scaly patch. The duration was one year. Cultures yielded hemolytic streptococci and beta hemolytic *Staphylococcus aureus*.

#### ETIOLOGY

During the past years several scrapings of the lesions have been made and a streptococcus was usually found. No records of these findings were made. During the past few months 7 cases of clinically typical eruptions were chosen at random, and cultures from scrapings of the lesions were made. The scrapings were cultured on Sabouraud's medium as well as blood agar and thioglycolate medium. In some of the cases repeated cultures were required before a positive growth was obtained.

Five of the 7 patients yielded hemolytic streptococcus on culture. One of these gave a growth of hemolytic *Staphylococcus aureus* in addi-

#### *Classification of Cultures from Seven Patients*

Patient Number	Age, Years	Duration, Months	Culture
1	7	6	Hemolytic streptococcus
2	12	3	Hemolytic streptococcus
3	18	12	Hemolytic streptococcus, hemolytic <i>Staph. aureus</i>
4	12	18	Hemolytic streptococcus
5	25	8	Hemolytic streptococcus
6	9	8	No growth (repeated cultures)
7	10	12	No growth (repeated cultures)

tion to the streptococcus. Cultures for the other 2 patients did not produce a growth. On several cultures there grew saprophytic fungi (*Aspergillus* and *hormodendrium*), but no pathogenic fungi were found. Scrapings were negative for *Malassezia furfur* in all cases.

#### HISTOPATHOLOGY

Unfortunately, the cases of early dermatitis, which precede the depigmentation, are rarely seen and are usually not properly diagnosed. It appears that a biopsy during this stage would reveal the usual changes associated with a superficial dermatitis. The earliest biopsy specimen that we have been able to obtain was from a scaly depigmented patch which was present for about two and one half months. The slide was examined by Dr. Fred Weidman, who reported his observations as follows:

Almost all pigment has disappeared, certainly for a Negro person. The reaction here is expressed, first, in the form of epithelial hyperplasia not alone in the epidermis but also in the hair follicles, second, in the form of the perivascular round cell infiltration (moderate), and, finally, in the form of parakeratotic changes on the surface. A high grade edema is added to the epithelial hyperplasia and parakeratosis. This edema affects both the epidermis and the subpapillary part of the corium.

A biopsy in a case of six months' duration showed similar changes but not so acute as those described in the first case, of two and one half months' duration.

Biopsy of a depigmented smooth lesion of one year's duration was reported by Dr. Weidman as follows:

The epidermis is normal in all respects. The character of the pigment is normal in all respects and normal in amount, at least on the basis of that of a white person. After that, the question of pigmentary abnormality must rest on the degree of "brunetism" in this particular patient. The most spectacular feature on the cutaneous surface is a dilated follicular orifice, but its contents are of a loose type. This speaks against a fundamentally keratosing process and more in favor of some passively dilating cause in the premises.

In the corium there are not any spectacular changes. At one end of the section the collagenous bundles are widely separated as by edema, such changes being confined to the upper half of the corium. There are not any inflammatory cellular infiltrations of any importance associated with this area. The latter cellular infiltrations are distributed from end to end in the section, when present at all, and occur as usual around the blood vessels.

Hair follicles appear to be normal. Sweat and sebaceous glands were not included in the sections studied. Only lymphocytes are concerned in the cellular infiltrate.

#### TREATMENT

One of us (J. J.), who has seen and treated numerous patients in the clinic as well as in private practice, prefers to use a crude coal tar ointment. In the dermatologic clinics juniper tar and ammoniated mercury ointment (ten per cent) are being used. All these drugs seem

to be effective if properly used. The patients are instructed to rub the salve into the lesions vigorously twice a day. The tar ointment is used until the pigmentation starts recurring. This usually takes three months. When ammoniated mercury ointment is used, a month's treatment is prescribed and then a rest period of two months. At the end of this time the pigment usually begins to reappear in the lesions. The ammoniated mercury ointment acts as a bleaching agent in some cases and therefore may prove not as desirable as the crude coal tar or the juniper tar.

#### PROGNOSIS

We have not seen any cases in which the disease did not respond to treatment if the salves were properly applied over a prolonged period. It seems essential that the treatment be continued for several weeks. In clinical practice the proper instructions are often not carried out, and failures should be expected.

#### COMMENT

The persistence of infection in the superficial layers of the skin is among the curious occurrences in dermatology. The commoner infections of this type are those caused by fungi. *Tinea versicolor* is a concrete example.

In 1923,<sup>5</sup> 1924<sup>6</sup> and 1925<sup>7</sup> Dr. Howard Fox presented several cases of partial depigmentation, chiefly of the face, in Negro children. The lesions started as red spots. In one to two weeks branny scaling would appear, but the lesions would gradually become smooth and partially depigmented. Cultures were negative for fungi. No bacterial growth was reported. The description of these lesions would well fit in with the disease that we have described as *erythema streptogenes*. Dr. Fox, in a personal communication, stated that he has seen the same clinical picture especially in dark-skinned persons (Negroes and Indians) in the West Indies and tropical parts of South America.

In 1924<sup>8</sup> V. Pardo-Castello and M. Martinez Dominguez described an eruption which affects the face and neck in the form of irregular macules and patches, slightly inflammatory, slightly scaly, of a dirty white color and somewhat itchy. The disease affects chiefly the face, particularly the cheeks, forehead and sides of the neck. The scales are furfuraceous, like fine dust adherent to the surface. The older lesions

5 Fox, H. Partial Depigmentation, Chiefly of the Face, in Negro Children, *Arch Dermat & Syph* 7 268 (Feb.) 1923.

6 Fox, H. Partial Depigmentation of the Face of a Negro, *Arch Dermat & Syph* 10 78 (Jul.) 1924.

7 Fox, H. Partial Depigmentation of the Face and Arms, *Arch Dermat & Syph* 12 753 (Nov.) 1925.

8 Pardo-Castello, V., and Martinez Dominguez, M. *Achromia Parasitaria*, *Arch Dermat & Syph* 9 82 (Jan.) 1924.

are devoid of scales. The lesions develop rapidly. The spread is considerable in a few days and may cover the body in a few weeks. An aspergillus was isolated in 6 of 36 cases. However, the importance of finding this common saprophyte is questionable in regard to the causation. The name attached to this eruption was *achromia parasitaria*. It was resistant to treatment although in some instances it responded to strong parasitocidal remedies.

Some of Pardo-Castello's cases compare well with our cases of *erythema streptogenes*. However, *erythema streptogenes* seems to spread slowly and rarely is widespread. We have seen several cases of partial depigmentation of the skin which covered extensive areas, was of long standing and failed to respond to treatment. No bacteria or parasitic fungi could be cultured. To these cases we still attach the term "*achromia parasitaria*."

The question arises as to whether the streptococcus found in these lesions plays a dominant or a contributory part in the production of the lesion.

Haxthausen<sup>9</sup> was able to find streptococci on normal skin in 7 out of 92 persons. Sabouraud<sup>10</sup> contended that the streptococci obtained from normal skin can never be considered as saprophytes. Further confirmation of this conclusion is given by the work of Dold,<sup>11</sup> who divided the reactions of laboratory animals to streptococci into three types: (1) *erythema*, more or less extensive with absence of infiltration, (2) severe inflammatory reaction, with infiltration and sharp demarcation of deep chronic necrotic process, and (3) rapidly extending cellulitis, with death of the animal within a few days. With these three types of reactions in mind, the Lévinés and Rabinowitch<sup>12</sup> investigated the pathogenicity of streptococci isolated from the normal skin of 15 persons. Of these strains twelve produced a reaction of type 1, and three strains produced a reaction of type 2. The conclusions arrived at were as follows:

- 1 Streptococci on the normal skin of persons in good health can never be considered as saprophytic.

- 2 There is a difference in the virulence of streptococci found on the normal skin.

The persistent finding of a hemolytic streptococcus in *erythema streptogenes* is undoubtedly a clue favoring this organism as the etiologic agent. The streptococcic dermatitis as described by Kinnear<sup>1b</sup> yielded a nonhemolytic streptococcus.

<sup>9</sup> Haxthausen, H. *Ann de dermat et syph* 8 201, 1927.

<sup>10</sup> Sabouraud, R. *Ann de dermat et syph* 8 321, 1927.

<sup>11</sup> Dold, H. *Zentralbl f Bakt (Abt 1)* 127 367, 1933.

<sup>12</sup> Lévine, E. M., Lévine, J. M., Levine, M. M., and Rabinowitch, M. S. *Ann de dermat et syph* 5 849, 1934.

Sabouraud suggested that all epidermic streptococcus infections which have not already been given a definite classification should be called *streptococcides eczematiformes*. The term "erythema streptogenes" was employed in this paper because the name has been used in our locality for many years when one is referring clinically to the described disease, erythema, not a trunk dermatitis, was the presenting feature. Even though erythema is only of short duration, it apparently always precedes the depigmentation. The disappearance of pigment is common to a number of inflammatory dermatoses when they are in the more acute stages. Dr. Fried Weidman commented personally to us that, observed histologically, when the epidermal cells were preoccupied, so to speak, with their business of proliferating, the normal and usual function of pigment production was often held in abeyance, and that this also holds true clinically. Those of us who frequently deal with dermatologic problems in the Negro race realize that a postinflammatory depigmentation is of rather common occurrence. In erythema streptogenes the streptococcus is apparently the exciting agent, however, the depigmentation should not be regarded as peculiar to the action of the streptococcus.

The fact that cultures of materials from 2 patients who had their lesions for eight and twelve months respectively failed to yield pathogens was interesting. Clinically the lesions were typical. The biopsy report for 1 patient who had the eruption for one year was given. This report as given showed essentially a normal picture. Only a slight non-inflammatory edema of the corium was present. This particular case is also the one in which the culture was negative. The eruption was treated with juniper tar (10 per cent) and cleared up in three months. From these observations one would expect the eruption to have been receding at the time that treatment was begun. Erythema streptogenes is a chronic dermatosis, but in some cases it is apparently self limited and disappears after several months or several years' duration even if not treated. The negative cultural and microscopic observations would support this clinical observation.

#### SUMMARY

1. A streptococcic dermatosis is described which is characterized by erythema followed by partial depigmentation. A hemolytic streptococcus is regarded as the etiologic agent.

#### ADDENDUM

Four additional cultures grew hemolytic streptococci in 1 case, hemolytic Staph. aureus in 1 case and hemolytic Staph. albus in 2 cases. The staphylococcus may also prove to be a factor in this disease. Tyrothricin ointment was found very effective as a treatment in 2 cases.

## EXAMPLE OF NEED FOR DERMATOLOGIC PUBLICITY OF DEVELOPMENTS IN RADIOLOGIC PHYSICS

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AND  
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**D**ERMATOLOGISTS throughout the world should profit from the discussion prompted by Dr C E Eddy's article in the April 1944 number of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY on "Calibration of X-Ray Equipment for Superficial Therapy," in which he criticizes certain statements we made in our paper on "Threshold Erythema Dose of Roentgen Rays" published in this same journal in March 1942

We stated that one of us (Belisario) had purchased a Victoreen dosimeter in the United States, and that it had been calibrated at the factory, again in Los Angeles and finally in Sydney, and that all comparisons agreed within a few per cent. We stated that "apparently for the first time a direct check of the dosage in Australia was obtainable for comparison with that employed in the United States, at least as far as the physical measurements are concerned," and that the conclusions of our paper would not be subjected to the criticism by clinicians that possibly the measurement of dosage might have varied in the different countries covered by the survey.

Dr Eddy's thesis was that the international roentgen unit had been satisfactorily established to within 0.5 per cent in Australia by 1937, that a well staffed, well equipped organization was prepared to calibrate x-ray equipment in the field under the auspices of the (Australian) Commonwealth Department of Health, and that the availability of this service had been widely publicized, as evidenced by his dozen or so citations from the literature.

The first comment we should like to make, and which we hope will be of benefit to all dermatologists, is that not a single one of the references which Dr Eddy cited could be reasonably assumed to be available to dermatologists: all of the references were to journals concerning radiology, cancer or physics. Medicine has become so specialized, and developments in each specialty are so numerous, that a physician cannot possibly cover much more than the literature in his own field. We hope, therefore, that this incident will result in making

available in the dermatologic journals all physical developments with which dermatologists should be familiar, this applies to the United States and other countries, as well as to this specific Australian instance in question. When the survey was made in Australia (1938) many of the dermatologists had not had a physical calibration of their equipment, very few had dosimeters, and they were not aware of any facilities for having this service performed for them.

The second point we wish to emphasize is that the very purpose of our paper was to discuss the relationship between the biologic reaction to the erythema dose and the physical dose measured in "roentgens." The fact that dermatologic radiation therapy practice was originally established more or less on the foundation of the erythema dose made a correlation between this biologic unit and the physical dose determination in "roentgens" most desirable in making the transition between the two methods.

The relative simplicity of irradiation in dermatology, compared to the complex problems of tissue doses at various depths which are encountered in "deep" therapy of deep-seated lesions, has resulted in neglect of the dermatologic field as far as radiation physics is concerned. The principal problem here is to determine the optimum surface dose which will achieve the desired result, this would be facilitated by a uniform dosage method, and we hoped that our paper would stimulate an interest in more exact data on dosage, directly or indirectly. Since the more difficult problems in radiation physics have been in the field of "deep" therapy (200 kilovolt range), most of the papers on this subject have been published in the radiologic journals. Dr Eddy states that his "attention (was) directed to" our article, implying that he was not in the habit of reading the *ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY*, just as dermatologists are not in the habit of reading the journals he cited in his references.

We believe that the average dermatologic clinician would be reassured by our statement regarding the comparison of the clinical dosimeter in the field, when he was unaware of any more exact standards and facilities in Australia due to lack of publicity in his literature. Our paper was essentially clinical, and was intended to correlate the clinical biologic reactions with the physical dose as used in practice in the field, not a physical discussion of the "roentgen."

Dr Eddy mentions that dermatologists in general accepted physical methods of measurement somewhat later than did "radiotherapeutists", since the latter term would apply to any physician using radiation therapeutically, presumably he is referring to radiologists and specialists in cancer who use radiation of higher voltage (200 kilovolt range) for the treatment of lesions at various depths in the body—not strictly sur-



face lesions, as in dermatologic practice. The fact that dermatology is concerned only with the surface makes it unnecessary for the dermatologist to have the same training in radiation physics that is required for the complex problems of high voltage therapy. For this reason it would not be logical to have the same type of papers on physical principles published in the dermatologic papers as appear in the radiologic journals, but we feel that developments of interest to them, announcements, and an occasional less technical article on the physical principles applicable in surface radiation therapy should be made available to dermatologists. We wrote our article for the clinician and realized that it would appear oversimplified to a physicist, but due to the different backgrounds of the two fields the same article could hardly be equally suitable for both.

Unfortunately Dr. Eddy's article might be interpreted as implying a controversy, in reality, such a dispute is nonexistent. Actually four different professions are involved in this subject of dosage, and all four are mutually interdependent, although not necessarily primarily interested in the same aspects of the subject.

- 1 Dermatologists, who are practicing medicine, and treating disease in the skin and superficial layers of tissue in the human body by means of roentgen rays

- 2 Radiologists and specialists in cancer, who are practicing medicine and treating disease throughout the body, including the cutaneous surface

- 3 "Clinical" radiation physicists, working in the field and advising the practicing physician in the accurate application of radiation in therapeutics and calibrating x-ray equipment, they must be familiar both with theoretic physics and with the problems of the physician who is not, and should not be expected to be, a professional physicist

- 4 Laboratory and theoretic physicists, in the standardization laboratories, and similar institutions, who control the accuracy of the international "roentgen" unit and maintain a standard (primary) against which clinical dosimeters may be compared under controlled conditions

One of us (J. C. B.) has corresponded at some length with Dr. Eddy, and this correspondence was seriously considered in preparing this article. We wish to emphasize that our statement was that Belisario obtained a "direct check of the dosage" in use in the two countries, not "the roentgen" as Dr. Eddy stated in his paper. The latter refers to the primary standard, of interest to profession no. 4, which is vital to international accuracy of dosage, and we are glad that the Australian facilities along this line have finally been publicized in a dermatologic journal. However, since dermatologists were apparently not previously aware of these facilities we believe that the operation of a single specific

dosimeter (secondary standard) by a single individual under identical conditions and technic on two continents would be reassuring to the clinical dermatologist in practice. It is to be hoped that Australian dermatologists will avail themselves of the facilities for calibration since no other method of dosage control affords comparable accuracy.

Physicists would not be impressed by considerations of the erythema dose, but since dermatologists are only gradually, and fairly recently, tending to shift to physical measurement it has real meaning to them, and it would be vain to ignore it. Besides making pertinent physical developments available to dermatologists, they should also be informed of the basic rationale of radiation physics since otherwise allusion to such facilities and developments would mean little to them. Such information should be provided in suitable terminology, taking into consideration that the dermatologist's surface irradiation does not necessarily require the same degree of understanding of radiation physics that is necessary for the complex problems of high voltage therapy.

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# FAMILIAL BENIGN CHRONIC PEMPHIGUS

## Report of a Case

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MONROE, MICH

AND

STEPHAN EPSTEIN, M D

MARSHFIELD, WIS

FAMILIAL benign chronic pemphigus (Hailey and Hailey's disease) is a rare dermatosis. Its cause is, as yet, not known. The following case is reported chiefly on account of the pathologic interpretation and the response of the lesions to therapy.

## REPORT OF CASE

*History*—Miss H. H., a white woman, aged 27, was referred to one of us (S. E.) on June 17, 1944, on account of a long-standing dermatosis of the neck.

Since childhood the patient had noticed a brown discoloration on both sides of the neck. For about eight years one of these areas usually had been sore. The eruption starts with little papules and blisters, later oozing occurs and crusts are formed. Some pruritus was constantly present. The lymph nodes of the neck were enlarged and tender during the time the eruption was active. For a few months of the year the lesions seemed virtually healed. This happened for the last time in the early months of 1944. Actually, the eruption never disappeared completely.

A sister, 22 years of age, has a similar eruption, but milder. In the last two years she had shown only pigmentation. This sister was also examined and presented more or less sharply outlined pigmented areas on both sides of the neck.

The patient presented sharply outlined lesions on both sides of the lower aspect of the neck. On the right side (fig. 1 A) there were numerous small blisters on top of erythematous areas. Some were filled with pus. Large crusted lesions were also present. These lesions occurred within an area of pigmentation. On the left side of the neck there was also pigmentation, and on top of it a somewhat infiltrated dermatitis resembling lichen simplex chronicus. This lesion was not so sharply outlined. The clinical picture was strongly suggestive of benign familial pemphigus.

The results of laboratory examinations were normal except for an eosinophilia of 6 per cent.

*Treatment and Course*—The patient was first treated locally with sulfanilamide ointment. This did not clear up the eruption, in view of the suggestion that the disease might be related to dermatitis herpetiformis, the patient was given sulfa-pyridine, 1 Gm. three times a day, later on, less. Under this treatment the lesions cleared up completely (fig. 1 B). However, whenever the patient ceased taking

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sulfapyridine for three days she noticed a burning and itching sensation and also a slight eruption at the usual sites. This always disappeared when she resumed the medication. In September 1944 sulfapyridine was discontinued and the skin became more itchy and a new eruption of blisters occurred. When seen on October 3 several crusted lesions were present on the right side. A biopsy was performed, and it was found that the uppermost layers of the skin came off with even slight pressure of a sharp knife. At that time treatment with vitamin A was started, 100,000 units a day. The eruption cleared up again and has not recurred to the date of this report, although the patient has discontinued the vitamin A medication since December 1944.

*Pathologic Observations (H P)*—The sections of skin (fig 2) show normal epidermis in a few small areas which are at most two or three papillae wide and surround hair follicles and sweat ducts. The pathologic changes start at a sharp line and involve all epidermal layers except the stratum corneum which remains

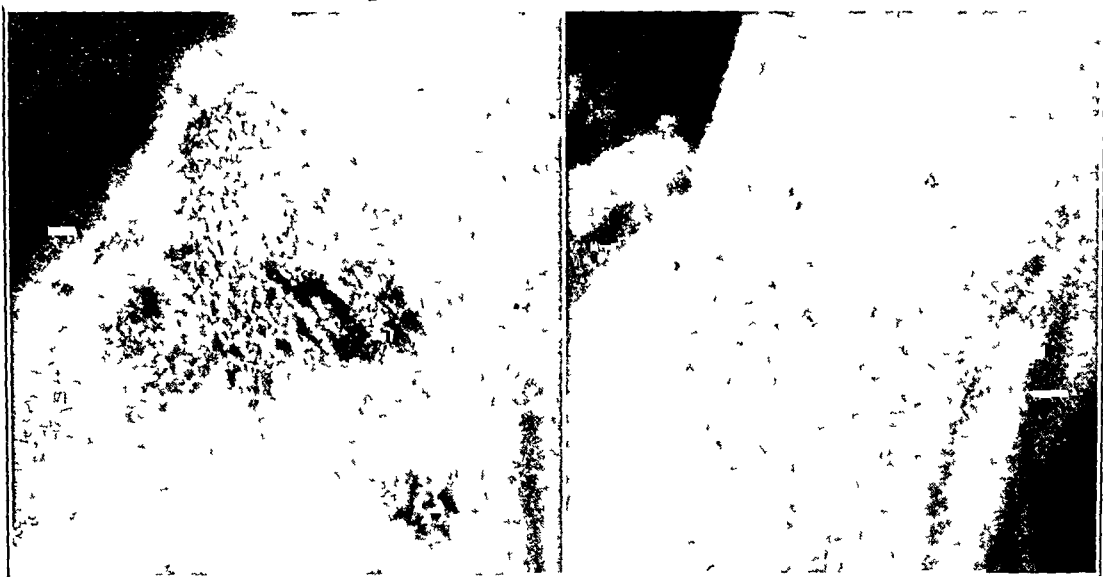


Fig 1—Appearance of lesion (A) before treatment, (B) after treatment with sulfapyridine. Note persisting pigmentation.

normal. The width of the epidermis is increased two or three fold, due partly to a greater number of cells, partly to an increase in size of the individual cells, and partly to the formation of clefts and spaces between the cells. The cytoplasm is augmented slightly without alteration in staining quality. The nuclei are definitely larger than normal and remain spherical even in the stratum granulosum. The clear perinuclear zone of endoplasm is decreased or completely absent.

Most spectacular are the changes in intercellular relations, the cells of the suprabasal layers lose most or all of their intercellular bridges, and many become completely separated and spherical. The higher strata of the rete show better cohesion and the granular and horny layers are normal with the exception of one small area where the surface of the skin has been broken and the entire epidermis is transformed into a pyknotic crust. Some areas show mere separation of the cells of the lower rete under preservation of gross architecture. In other spots, one finds clefts and spaces in which rounded epithelial cells are suspended, in still others,

lakelike intraepidermal vesicles have formed which contain, in addition to epithelial cells, a granular precipitate and polymorphonuclear leukocytes (fig 2 A) These alterations are accompanied by increased size and budding of the rete ridges (fig 2 C) which compress the papillae between them and undercut the normal epidermis to some extent Mitotic figures are rare

The acantholytic cells (fig 2 B) are usually round and single, but some adhere to others with broad flattened surfaces and may form mulberry-like clumps One instance of so-called pseudophagocytosis was seen, one spherical cell being partly surrounded by a bowl-shaped second one (fig 2 D) Binucleate cells occur among the free elements, and multinucleate cells are relatively frequent in the coherent upper strata of the rete Some of the spherical cells contain pigment granules, many retain remnants of tonofibrils in the cytoplasm Most of the cells stain normally, but some become more acidophilic and hyalinized, while their nuclei become hyperchromatic and large No definite evidence of keratinization of individual cells is found Neither the upper strata of the rete nor the horny layer contain any dyskeratotic cells

The corium is somewhat edematous in its upper third The blood vessels are wide and contain neutrophilic granulocytes There is a moderate amount of perivascular round cell infiltration Some plasma cells, a few mast cells and a fair number of melanophores are present The elastic fibers are diminished in number The epidermal appendages are normal

#### COMMENT ON MICROSCOPIC OBSERVATIONS

The histologic picture is similar to that first described by Pels and Goodman<sup>1</sup> and by Hailey and Hailey<sup>2</sup> and designated as a bullous variety of Darier's disease and as chronic benign pemphigus respectively Practically identical findings were reported by later observers of similar cases, and our case adds nothing basically new There are a few details, however, concerning which our observations may be helpful

1 There is remarkable morphologic similarity between the acantholytic areas of our specimen and the changes which normal epidermis undergoes in tissue culture outside the body<sup>3</sup> In either case the cells break off the bridges which tie them to their neighbors, but may retain remnants of tonofibrils in their bodies They become spherical, but may reassociate by flattening out against one another or by partly surrounding others (pseudophagocytosis) In tissue culture these changes are not signs of degeneration, but of increased individuality The cells may, under certain conditions, reorganize into a tissue and form

1 Pels, I R, and Goodman, M H Criteria for the Histologic Diagnosis of Keratosis Follicularis (Darier), *Arch Dermat & Syph* **39** 438 (March) 1939

2 Hailey, Howard, and Hailey, Hugh Familial Benign Chronic Pemphigus, *Arch Dermat & Syph* **39** 679 (April) 1939

3 Pinkus, H (a) Ueber Gewebekulturen menschlicher Haut, *Arch f Dermat u Syph* **165** 53, 1932, (b) Notes on Structure and Biological Properties of Human Epidermis and Sweat Gland Cells in Tissue Cultures and in the Organism, *Arch f exper Zellforsch* **22** 47, 1938



Fig 2—Sections (*A* and *B*) stained with acid orcein and Giemsa solution, (*C* and *D*), stained with hematoxylin and eosin. (*a*) Thickening of the epidermis, suprabasal clefts and large intraepidermal vesicle. Between the arrows there is a short stretch of normal epidermis. (*b*) Detail of acantholytic vesicle. Normal epidermis of the surroundings of a hair follicle ends at the points indicated by the arrows. The lower arrow also indicates the tip of the elongated cutaneous papilla separating normal and pathologic epithelium. *X* marks the extreme tip of the budding acantholytic rete. Note difference in the size of normal and pathologic nuclei and almost complete absence of the perinuclear light area in the intraepidermal cleft, (oil immersion lens), *a*, acantholytic suprabasal zone, *p*, pseudophagocyte in the intraepidermal cleft, *b*, binucleate cells in the upper half of the epidermis connected to each other and their neighbors by intra-cellular bridges. *K*, keratohyaline layer.

bridges and a system of tonofibrils. Something similar appears to be true in our case in which the cells after passing through a labile period in the suprabasal stage of their lives, regain cohesiveness in the higher strata.

The alterations of the explanted tissue are attributable to two causes: loss of the regulating influences of the organism and exposure to abnormal physicochemical conditions. Neither factor can be regarded as responsible in our case. The tissue remains in the body, and any general physicochemical differences in the surroundings ought to affect the circumfollicular epithelium as well as the rest of the epidermis. One would not expect such a sharp line of demarcation between normal and pathologic epithelium as actually exists in our sections. It appears, then, that the basic change must be in the epidermal cells themselves, which respond to normal stimuli in a faulty manner.

2. The principal disagreement of previous authors has centered on the question whether the disease is a variety of keratosis follicularis or an entirely separate entity. Of the four features which characterize the histologic picture of Darier's disease—hyperkeratosis, dyskeratosis, acantholysis and epithelioma-like basal cell proliferation, our specimen shows but two. There is a mild degree of basal cell proliferation discernible mainly at the edge of the lesion where the rete buds undercut the normal epidermis. Acantholysis is excessive, leading to complete disruption of the epidermis and to vesiculation. The presence of dyskeratosis is questionable if this term is understood to mean that individual cells undertake the specialized function of keratinization in a faulty manner and is not vaguely used for any kind of cellular degeneration. Hyperkeratosis is absent.

It appears, then, that two features of Darier's disease are lacking. This cannot be explained by the acuteness of the process. While Frank and Reim<sup>4</sup> have shown that vesicles may occur within a few hours, there is ample evidence in our sections that the basic alterations of the epidermal cells have been present for a long time. The budding of the rete ridges is a chronic process requiring more time than the development of a hyperkeratotic horny layer. Also, the presence of numerous binucleate and multinucleate cells in the upper strata of the epidermis shows that cell life has been abnormal before acantholysis became manifest. The time required for the formation of binucleate prickle cells should be plentiful for keratinization of individual cells. It is also noteworthy that in our sections the circumfollicular and circumporal epithelium is the only part of the epidermis free of pathologic

<sup>4</sup> Frank, S. B., and Reim, C. R. Dyskeratoid Dermatitis, *Arch. Dermat. & Syph.* 45:129 (Jan.) 1942.

changes. The significance of follicular involvement in Darier's disease is still under discussion. Ellis,<sup>5</sup> in a recent study, states the belief that it only incidentally affects the hair follicles. While Darier's disease is not always follicular, lesions have been found even in the stratified squamous epithelium of mucous membranes<sup>6</sup>—the cutaneous appendages appear to be at least favorite centers of the lesions in keratosis follicularis.

#### SUMMARY AND CONCLUSIONS

A case of familial benign chronic pemphigus (Hailey and Hailey's disease) is presented. Clinically and histologically the case fits in well with those previously reported. The patient responded well to treatment with sulfapyridine at one time, and vitamin A at another time. Little is known about the treatment of this disease with sulfonamide compounds. The disease in Lynch's<sup>7</sup> patient responded to sulfathiazole. Although no definite conclusions can be drawn because spontaneous remissions are frequent in this disease, the prompt disappearance of subjective symptoms and the healing of visible lesions after two so widely different therapeutic agents are of interest because of the suggested relation of Hailey's disease to pemphigus and dermatitis herpetiformis on the one hand and to keratosis follicularis on the other.

The relation of the disorder to Darier's disease is discussed. Our case bears out the experience of other observers that this disease is chronic and recurrent rather than progressive as is Darier's disease. In spite of many years' duration, the changes remain superficial and flat, and the vegetating lesions, so characteristic of keratosis follicularis, never develop.

The histopathologic process is characterized by budding of the epidermal ridges and by acantholysis leading to the formation of intra-epidermal clefts and vesicles. The cutaneous changes appear to be secondary. The designation of chronic recurrent acantholysis fits the histologic picture better than either benign pemphigus or bullous dyskeratosis. Although our sections resemble Darier's disease more closely than any other dermatosis, we do not believe that the two conditions should be identified, at least not with our present knowledge.

5 Ellis, F. A. Keratosis Follicularis Is Not Primarily a Follicular Disease, *Arch. Dermat. & Syph.* **50**: 27 (July) 1944.

6 Brunauer, S. R. Morbus Darier, in Jadassohn, J. *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1931, vol. 8, pt. 2, p. 230.

7 Lynch, F. W. Benign Pemphigus (Hailey and Hailey) Treated with Sulfathiazole, *Arch. Dermat. & Syph.* **43**: 736 (April) 1941.



## FIXED SULFATHIAZOLE ERUPTION OF UNUSUAL DISTRIBUTION

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FIXED eruptions due to sulfanilamide<sup>1</sup> and sulfathiazole<sup>2</sup> have been reported but appear to be a relatively rare toxic manifestation of the sulfonamide drugs. Like those observed commonly with phenolphthalein,<sup>3</sup> antipyrine and the arsphenamines,<sup>4</sup> the reported cases consisted principally of brownish to black macules of the skin surface, which became inflamed when the causative drug was administered.

The purpose of this paper is to report a case of fixed eruption due to sulfathiazole, distinguished by the peculiar distribution of the lesions.

### REPORT OF A CASE

*History*—A Negro, aged 29, was admitted to the hospital on April 14, 1945, complaining of painful raw areas of the lower lip, the mouth and the glans penis. The lesions were approximately two days old and had appeared within forty-eight hours after the ingestion of 4 Gm of sulfathiazole as a venereal prophylactic.

The patient first began using sulfathiazole as a venereal prophylactic in 1942. He customarily took 2 Gm of the drug before and after each exposure. This dose was taken three or four times each month, without apparent toxicity, and without the development of venereal disease.

In October 1944, in New Guinea, the patient suffered a severe laceration of the back of the neck. He was hospitalized, and the wound was sutured under general anesthesia. Postoperatively he was given sulfathiazole orally, but he does not know whether sulfathiazole powder was dusted into the wound. Nevertheless, the application of sulfathiazole powder to dirty wounds is such common practice that,

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1 Loveman, A. B., and Simon, F. A. Fixed Eruption and Stomatitis Due to Sulfanilamide, *Arch. Dermat. & Syph.* **40**: 29 (July) 1939. Goodman, M. H., and Arthur, R. D. Fixed Eruptions. Report of an Unusual Condition Due to Sulfanilamide, *ibid.* **43**: 692 (April) 1941. Dostrovski, A., and Sagher, F. Fixed Erythema Due to Sulfanilamide with Gradually Lessening Sensitivity, *ibid.* **49**: 418 (June) 1944.

2 Director, W. Fixed Eruption, Conjunctivitis and Fever from Sulfathiazole, *Arch. Dermat. & Syph.* **48**: 523 (Nov.) 1943.

3 Abramowitz, E. W. Fixed Eruptions from Various Drugs and Other Agents, *Arch. Dermat. & Syph.* **43**: 672 (April) 1941.

4 Chargin, L., and Leifer, W. Fixed Eruptions Due to the Arsphenamines, *J. Invest. Dermat.* **3**: 443 (Dec.) 1940.

especially in the light of subsequent events, it may be assumed that this was actually done. During hospitalization a raw, sore area developed on the glans penis. Studies for venereal disease proved negative, and the lesion healed spontaneously in a few days, leaving a residual spot of darkened skin.

Shortly thereafter the patient was returned to the United States, and in March 1945, for the first time since the accident in New Guinea, he took sulfathiazole as a venereal prophylactic. Within forty-eight hours the original area on the penis became raw and painful, in addition, the lower lip became puffy and blistered, and there was soreness of the mouth. These lesions healed rapidly without treatment.

Just prior to the present admission to the hospital the patient had once again ingested 4 Gm of sulfathiazole.

*Examination*—Lesions were present on the tongue, hard palate, lower lip and penis. On the dorsum of the anterior portion of the tongue was a large, sharply demarcated, reddened plaque, which was almost completely denuded of papillae. There was a coinlike, roughly round, red, eroded area of the mucosa of the hard palate, about which was some brownish black pigmentation. The lower lip was diffusely swollen, as in angioneurotic edema, and there were two discrete eroded areas about 5 mm in diameter. Except for two small normally pigmented areas the entire lower lip was almost black, far darker than the unaffected upper lip. A crescent of blackish pigmentation was present on the chin, contiguous with the vermilion border of the lip, and apparently was a direct extension from the lesion of the lip. On the proximal portion of the glans penis, extending across the sulcus onto the mucosal surface of the prepuce, was an oval pigmented lesion. The discoloration was most intense on the glans and faint on the prepuce. The entire lesion was moderately edematous, it was reddened at part of its periphery, and at one point contained a crusted erosion. All the lesions subsided gradually without therapy, leaving residual pigmentation of the lip, palate and penis.

*Laboratory Data*—The Kahn test of the blood was negative. The hemogram showed 8,450 white blood cells, with 64 per cent polymorphonuclear leukocytes, 2 per cent eosinophilic leukocytes, 33 per cent lymphocytes and 1 per cent mononuclear cells. The urinalysis gave normal results.

*Course*—When the active lesions had subsided completely, sulfadiazine, 0.25 Gm, was given orally, following which the patient experienced burning and tingling sensations in the eruptive areas, but no objective change was noted.

At a later date, sulfathiazole, 2 Gm, was administered by mouth. This was followed not only by characteristic flaring of the original lesions but also by the appearance of two new lesions. One of these involved the scar of the old laceration that extended horizontally for about 18 cm across the back of the neck. All the skin adjacent to this scar, and extending outward from it for some 5 to 10 mm, became puffy and red, and clusters of vesicles appeared at several points. This entire region burned and itched intensely. An oval, edematous, red area, about 1 by 2 cm, appeared in each palm, and later the superficial layer of skin desquamated from these lesions.

Once more all lesions were allowed to return to normal, except for residual pigmentation, and then another oral dose of sulfathiazole was administered. Within forty-eight hours there was activation of all former sites of eruption on the tongue, palate, lower lip and penis. Again the skin about the scar on the neck became inflamed and vesicular, and the palmar spots became itchy and were surrounded by a halo of redness.

An intradermal test for sensitivity to sulfathiazole was performed on the forearm, according to the technic of Leftwich,<sup>5</sup> with negative results

Five per cent sulfathiazole ointment was applied to an unaffected area on the left forearm, the scar of the neck and the pigmented spot on the glans penis for three consecutive days. No subjective symptoms or objective change occurred

#### COMMENT

Fixed eruptions confined to the lips, mouth and/or penis have been observed with phenolphthalein and the barbiturate drugs. This distribution of a fixed eruption after the sulfonamide drugs must be decidedly rare, especially in view of the tremendous amounts of these drugs that have been used

The mucosal lesions in this case are the result of hematogenous sensitization. The acute vesicular dermatitis about the scar of the neck is a fixed eruption in a different pathogenetic sense. The concept is that the cells about the scar were sensitized<sup>6</sup> by the direct application of sulfathiazole powder to the open wound, the eruption being elicited by oral administration of the drug

In so localized a form of hypersensitivity it is not surprising that the reaction to the intradermal test for sulfathiazole sensitivity was negative. It will be interesting to note in a more suitable case the effects of this test when performed within the area of fixed eruption

#### SUMMARY

A case of fixed eruption due to sulfathiazole is described. The unusual features are the limitation of the eruption to the lip, tongue, palate and penis, also the appearance of an acute vesicular dermatitis about an old scar after oral administration of the drug. The acute dermatitis is ascribed to local sensitization by direct application of sulfathiazole powder to the fresh laceration

5 Leftwich, W. B. An Intradermal Test for the Recognition of Hypersensitivity to the Sulfonamide Drugs, *Bull. Johns Hopkins Hosp.* **74**: 26 (Jan.) 1944

6 Shaffer, B., Lentz, J. W., and McGuire, J. A. Sulfathiazole Eruptions: Sensitivity Induced by Local Therapy and Elicited by Oral Medication, *J. A. M. A.* **123**: 17 (Sept. 4) 1943

# TREATMENT OF SEVERE PUSTULAR DERMATOSES AND STAPHYLOCOCCIC SEPTICEMIA BY ORAL ADMINISTRATION OF PENICILLIN

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IN THE following pages we report 2 severe cases of pyogenic dermatitis. The first case was one of a severe pyoderma of both hands, which was treated by the oral administration of penicillin following two relapses after sulfadiazine therapy. The second case was one of extensive pustular dermatitis, involving the hands, arm and legs. This case was complicated by a hemolytic staphylococcic septicemia.

## REVIEW OF EXPERIMENTAL WORK

The administration of penicillin by mouth has been ineffective due to the destruction of the antibiotic substance by the action of hydrochloric acid. This observation was made first by Abraham and Florey and their associates<sup>1</sup> and was subsequently verified by other investigators<sup>2</sup>. This was also proved clinically by Rammelkamp and Helm,<sup>3</sup> who administered penicillin by mouth to 2 patients with pernicious anemia and achlorhydria. Therapeutic blood levels were obtained in these patients. More recent efforts<sup>4</sup> have been made to overcome this major obstacle of inactivation by the hydrochloric acid, and most encouraging results have been achieved. The work of Gyorgy<sup>5</sup> and his associates was done by

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1 Abraham, E P, Florey, H W, Chan, E, Fletcher, C M, Gardner, A D, Heatley, N G, and Jennings, M A. Further Observations on Penicillin, *Lancet* **2** 177, 1941

2 Rammelkamp, C H, and Keefer, C A. The Absorption, Excretion and Distribution of Penicillin, *J Clin Investigation* **22** 425, 1943

3 Rammelkamp, C H, and Helm, J C, Jr. Studies on the Absorption of Penicillin from the Stomach, *Proc Soc Exper Biol & Med* **54** 423, 1943

4 Libby, R L. Oral Administration of Penicillin in Oil, *Science* **101** 178, 1945. Little, C H, and Lamb, G. Penicillin by Mouth, *Lancet* **1** 203, 1945. McDermott, W, Bunn, P A, Benoit, M, Dubois, R, and Haynes, W. Oral Penicillin, *Science* **101** 228, 1945. Burke, F G, Ross, S, and Strauss, C. Oral Administration of Penicillin, *J A M A* **128** 83 (May 12) 1945

using penicillin calcium orally with trisodium citrate as a buffer, as suggested by Charney, Alburn and Bernhart<sup>6</sup> Penicillin is most stable between  $p_H$  4.8 and 7.9 and is inactivated beyond this range

#### REPORT OF CASES

CASE 1—The patient (J. P.), a white man aged 34, was first seen May 8, 1945 while still in bed convalescing from an infection of the upper respiratory tract, which he had had for a week. His temperature and pulse rate were normal, and his general appearance good. His past history indicated that he had had apparent episodes of dyshidrosis. He presented many pustular lesions, ranging in size from 1 mm to 15 mm in diameter. Many of these lesions were excavating in character and covered extensive areas of the fingers, palms and backs of both hands. The lesions were tense, some were broken and oozing, and his hands were swollen and red. No visible lymphangitis was present, but axillary lymph nodes could be felt on palpation. Sulfadiazine in doses of 3 Gm per day, fluids, rest in bed and 1:2,000 solution of mercury bichloride wet packs were prescribed. The lesions gradually dried up and apparent cure took place in eight days, at which time no evidence of even the smallest pustules could be seen.

Four days later there was a decided recurrence of lesions and visible lymphangitis was seen, extending halfway to one elbow. Hospitalization with adequate parenteral penicillin therapy was considered, but because of economic considerations the original treatment was renewed. Within a week all lesions had completely dried up and again what appeared to be a complete recovery had taken place. In view of the first relapse, it was thought advisable to supplement this therapy with penicillin. The patient remained in his home and was given 20,000 units of penicillin intramuscularly every four hours during the day for two days, with a total dosage of 200,000 Oxford units.

Five days later there was complete recurrence of lesions on the fingers, palms and backs of his hands, with multiple lymphangitis extending up both forearms to the elbows. The patient had a noticeable pallor, his temperature was 102 F, and his pulse rate was 120 per minute. Further sulfadiazine therapy was deemed inadvisable, and hospitalization with adequate parenteral penicillin therapy was contemplated.

It was at this point that the oral administration of penicillin was decided on. This was done for several reasons. First, penicillin therapy is effective and safe in the treatment of pyogenic dermatoses.<sup>7</sup> Second, the parenteral administration of penicillin involves a rather elaborate and time-consuming procedure, of which hospitalization is usually a prerequisite. Third, oral therapy is easier and less disagreeable from the patient's standpoint. Fourth, recent studies show that the oral administration of penicillin has real promise in the effective treatment of infectious diseases.

5 Gyorgy, P., Vandegrift, H. N., Elias, W., Colio, L. G., Barry, F. M., and Pilcher, J. D. Administration of Penicillin by Mouth, *J. A. M. A.* **127**: 638 (March 17) 1945.

6 Charney, J., Alburn, H. E., and Bernhart, F. W. Urinary Excretion of Penicillin in Man After Oral Administration with Gastric Antacids, *Science* **101**: 251, 1945.

7 Herrell, W. E. Penicillin and Other Antibiotic Agents, Philadelphia, W. B. Saunders Company, 1945.

The patient was given penicillin calcium combined with sodium citrate<sup>8</sup> in the dosage given in the following paragraph. The approximate expected blood levels of penicillin following its oral administration had previously been determined by one of us (H G N)<sup>9</sup> on a small series of patients. At the time the penicillin was given cultures were taken from the lesions on the patient's hands. *Staphylococcus aureus* and beta hemolytic streptococcus were isolated. The strain of staphylococcus was coagulase positive. Blood cultures taken prior to the administration of the penicillin were negative.

The patient was given 10 penicillin calcium tablets (200,000 units) every hour for four doses or until 40 tablets had been taken. This was followed by 7 tablets every two hours for the first twenty-four hours. Thereafter 5 tablets were given every two hours during the daytime for the following fourteen days.

The results were altogether gratifying. Within eighteen hours after the initial oral dose of penicillin the patient's temperature had dropped from 102 to 98.6 F, and his pulse rate had dropped from 120 to 92 per minute. His general appearance was much improved, and the tense, swollen character of his hands had subsided. The patient also stated that he was feeling much better. At this same time the penicillin blood level was found to be 2.4 units per cubic centimeter of serum, following the method of Cooke<sup>10</sup>. This level is well above the therapeutic range of 0.02 to 0.2 units per cubic centimeter of serum as given by Kolmer<sup>11</sup>.

Owing to the decided clinical improvement, further penicillin blood levels were not ascertained. The patient steadily improved, and the temperature and pulse remained normal. No toxic effects of penicillin were noted. The pustular appearance of the lesions completely disappeared within a week, followed by subsequent gradual sloughing of crusts. Twenty-one days have elapsed since the patient has had any therapy, and he shows no evidence of recurrence of the eruption.

**CASE 2**—The patient (A W), a 20 year old white woman, was admitted to the isolation ward of St Margaret's Hospital, Kansas City, Kan., at 8 p. m. on June 13, 1945. On admission, examination revealed that the patient had pustular lesions covering extensive areas of the hands, arms, legs and thighs. These varied in size from 1 mm to 15 mm in diameter. Many of the pustules had coalesced, forming larger confluent lesions. Typical lesions are seen in figure 1.

The past history revealed that the patient had been working in a war plant for the past several months. She had been wearing clothing laundered with fire-protective processing, and about two weeks prior to the present illness a contact dermatitis developed on her extremities. The pustular lesions appeared three days prior to her admission to the hospital. While being transported in an ambulance from a nearby city she had several chills.

The patient presented a florid, toxic appearance. Her temperature was 104 F and her pulse rate was 120 per minute. She was listless. The blood count showed 19,000 white cells with 90 per cent polymorphonuclear leukocytes, 24 of which were nonfilamented. Urinalysis showed 10 to 15 red blood cells and 5 to 10 white blood

8 The penicillin calcium tablets combined with sodium citrate, each tablet containing 20,000 units, were kindly supplied by E. R. Squibb and Sons.

9 Nelson, H. G. Studies on the Oral Administration in Penicillin, *J. Kansas M. Soc.* **46**: 224, 1945.

10 Cooke, J. V. A Simple Clinical Method for the Assay of Penicillin in Body Fluids, *J. A. M. A.* **127**: 445 (Feb. 24) 1945.

11 Kolmer, J. A. Penicillin Therapy Including Tyrothricin and Other Antibiotic Therapy, New York, D. Appleton-Century Company, Inc. 1945.

cells per high power field. A blood culture taken at this time showed a pure culture of hemolytic *Staph aureus*. Cultures from the lesions on the skin showed these same organisms and in addition beta hemolytic streptococci.

The patient was given 10 penicillin calcium tablets every hour for four doses. The dose was then reduced to 7 tablets every hour for twenty-four hours. Following this the dose was reduced to 5 tablets every two hours during the daytime only. This regimen was continued for nine days, at which time the medication was stopped.



Fig 1 (case 2) —Pustular lesions on hands and arms. The lesions are equally numerous on the ankles, legs and thighs.

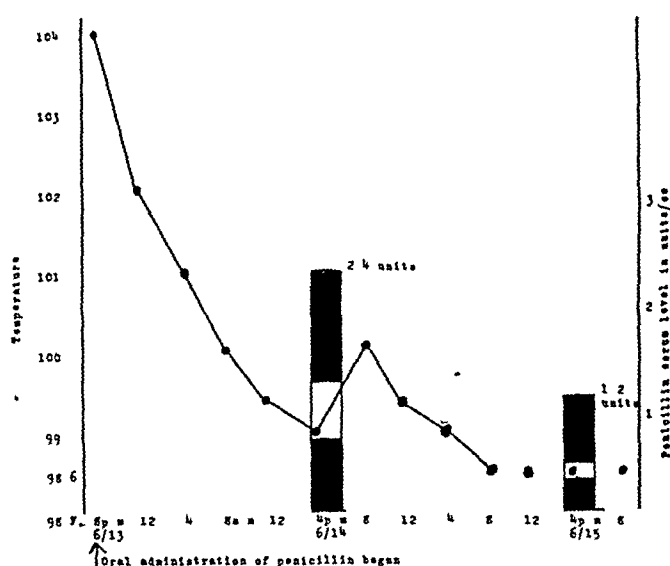


Fig 2 (case 2) —Simultaneous changes in temperature and in penicillin blood serum levels.

The temperature and penicillin levels are shown in figure 2. It is seen that the temperature dropped from 104 to 99 in eighteen hours. Within thirty-six hours the temperature was 98.6. The penicillin blood level was 24 units per cubic centimeter twenty hours after the initial dose was given. The second day after administration the level was 12 units, and the levels on the third, fifth and seventh days was 0.2 units per cubic centimeter.

Blood cultures taken twenty-four and seventy-two hours after admission were negative. The white blood count in forty-eight hours had dropped from 19,000, on admission, to 8,000 with 70 per cent polymorphonuclear leukocytes, 14 of which were nonfilamented. Five days after admission the white count was 7,000 with 58 per cent polymorphonuclear leukocytes, 6 of which were nonfilamented.

The patient's general condition showed remarkable improvement within twelve hours after the initial medication was given. By the end of five days after the penicillin was administered the pustules had completely dried up, leaving only scaling, yellow crusts. By the end of seven days the crusts had disappeared. The patient was dismissed from the hospital on June 23, 1945, ten days after admission.

It is our impression that the patients would probably have improved with smaller doses of penicillin than those given.

#### CONCLUSIONS

1 A patient with severe pustular dermatitis was treated successfully by the oral administration of penicillin, following two relapses with sulfadiazine therapy and intramuscular administration of penicillin.

2 A patient with severe generalized pustular dermatitis complicated by a hemolytic staphylococcic septicemia responded dramatically to the oral administration of penicillin.

3 No toxic effects from the penicillin were noted with the dosages given.

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# Clinical Notes

## CHEILITIS FROM LOCAL USE OF PENICILLIN SOLUTIONS IN MOUTH

### Report of a Case

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In the course of a study of the local effect of penicillin on chronic recurrent aphthous ulcers, a cheilitis was observed

The patient was a 61 year old white woman who had had recurrent ulcerations of the buccal mucosa, tongue and posterior wall of the pharynx for fifteen years. Periods of remission had lasted more than from two to two and a half weeks. Complete physical examinations, tests for allergy to foods and inhalants and all types of local and systemic therapies had been without help. There were no episodes of herpes simplex. The mouth was edentulous. Numerous painful shallow, sharply margined reddish ulcers, with intense red collars, were scattered over the buccal mucosa, under the tongue, about the gums and on the hard palate. There was no atrophy or scarring visible. A smear of material from the early lesions showed staphylococci and streptococci. No bacilli or spirillas were present. Smears of material from late lesions showed a similar picture. Cultures of material from early and late lesions showed hemolytic streptococci. No systemic therapy of any sort was being administered when use of a stable calcium penicillin ointment, 500 units per gram, was started. This was applied heavily with cotton applicators to each of the affected areas, after the ulcers were sponged with cotton. Applications of penicillin ointment were made three to four times daily. The ointment was kept at refrigerator temperature. Except for deep ulcers about the margins of the gums, the results in five days were excellent. No new lesions appeared, and the old ones improved remarkably. In one month the patient's lesions were healed except for one large linear lesion below the gum. Here, the application of the salve was difficult, and the pressure from the plate was great. As an attempt at prophylaxis, sodium penicillin solutions of another brand, 500 units per cubic centimeter of sodium chloride solution were freshly prepared, and the patient rinsed her mouth with this three times a day. There was no immediate discomfort from this, but in two days a vesicular cheilitis with considerable edema of the lips developed. The buccal mucous membranes were clear. There were no lesions on the face. Use of penicillin was stopped, and several fresh ulcerations appeared on both cheeks. Calcium penicillin ointment was started again, with improvement but not with complete healing. Patch tests were made, with the following results:

The reaction was negative to calcium penicillin ointment. There was a 2 plus reaction to sodium penicillin solution (500 units per cubic centimeter of sodium

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Stable calcium penicillin ointment was furnished by the Schenley Research Institute

chloride solution) There was a negative reaction to three other brands of sodium penicillin (2,000 units per cubic centimeter of sodium chloride solution)

Negative reactions were elicited by contact tests on the buccal mucosa<sup>1</sup> made with the following substances sodium penicillin solution (500 units per cubic centimeter, 1,000 and 2,000 units per cubic centimeter), calcium penicillin ointment and an acrylic resin denture

In addition, a stable calcium penicillin ointment was rubbed over the lips, and no reaction appeared When this was repeated with the sodium penicillin solution, edema of the lips occurred within twenty-four hours

In 4 other patients of the series with recurrent aphthous ulcers, no reactions occurred from the topical use of calcium penicillin ointment Contact tests on the buccal mucous membrane with the calcium penicillin ointment elicited negative reactions in 4 patients within the thirty minute testing period No determinations of the salivary concentrations of penicillin were made Penicillin lozenges or capsules as yet have not been tried No tests with purified crystalline penicillin or penicillin fractions were made

#### SUMMARY

In a patient under treatment with local applications of penicillin for chronic recurrent aphthous stomatitis, cheilitis developed when solutions of sodium penicillin were used as a mouth wash A stable calcium penicillin ointment produced no irritation and was of definite benefit Contact tests on the skin elicited a positive reaction to the solution, but there was no reaction to three other brands of sodium penicillin solution and the penicillin ointment Contact tests of the buccal mucosa elicited negative reactions both to the solutions and to the ointment Direct applications of sodium penicillin solution to the lips produced a cheilitis No reaction was produced on the lips by the calcium penicillin ointment

733 Carew Tower

1 Goldman, L., and Goldman, B Contact Testing of Buccal Mucous Membrane for Stomatitis Venenata, *Arch Dermat & Syph* 50 79 (Aug) 1944

### URTICARIA DUE TO TRINITROTOLUENE

J F PRESTON Jr, M D, and C A WATKINS, M D, CHATTANOOGA, TENN

The following unusual case of allergic reaction to trinitrotoluene is believed to merit reporting

#### REPORT OF A CASE

The patient, a 25 year old white woman, was employed in the production of trinitrotoluene as a wash house helper on Sept 20, 1944 Preemployment physical examination showed no abnormality except an amblyopic left eye The family and past histories revealed no allergic or dermatologic disease

On September 29, nine days after starting to work, she reported to the dispensary with an itching, vesicular eruption on the hands She was given calamine lotion, following which the eruption desquamated for about a week Although she continued on the same job, there was no recurrence of this type of dermatitis A patch test with trinitrotoluene was not done at this time since the appearance was typical of trinitrotoluene dermatitis, so commonly observed in the dispensary

On October 3, she came to the dispensary for treatment of a cold of one week's duration She had coryza and a severe, nonproductive cough Her temperature was 99.3 F She did not wish to go home as suggested She returned on October

11, 14, 15 and 16, complaining of almost constant cough. On these occasions physical examination of the chest showed no abnormality. She ignored repeated advice to stay home, but took various medications. The known medicaments she received are the following: elixir of terpin hydrate with codeine, compound tincture of benzoin as a steam inhalation, a proprietary cough medicine containing potassium iodide, lozenges containing a local anesthetic and an organic iodide, and aspirin compound capsules containing acetylsalicylic acid, phenacetin and caffeine.

On October 23, she reported with a generalized urticaria which responded promptly to 1 cc of a 1:1,000 solution of epinephrine. She was given ephedrine and pentobarbital sodium capsules to take every four hours, if needed. The following day she reported with a recurrence of the urticaria, accompanied by swelling of the eyelids, lips and tongue, lacrimation, nausea and vomiting, dyspnea and increased coughing. Examination revealed generalized urticaria accompanied by small petechiae, most prominent in the axillae, and a number of small purpuric spots. The oral mucous membranes appeared normal. There were erythema and edema of the eyelids and a thin, nasal discharge. Throughout both pulmonary fields were musical rales of an asthmatic character. The Rump-Leeds capillary fragility test produced no petechiae. The temperature was 98 F, the pulse rate 76, the blood pressure 110 systolic and 80 diastolic. The laboratory data were as follows: At the time of the preemployment examination, Sept 16, 1944, hemoglobin was 15.4 Gm, the cell volume by the Wintrobe hematocrit test 41, and reactions to the Kahn precipitation and the Kline flocculation tests were negative. Urinalysis did not reveal sugar or albumin. Roentgen examination of the chest was made on September 16 and showed no abnormalities of the heart or lungs. On November 6 hemoglobin was 13.7 Gm and cell volume 41.

She was instructed to discontinue all medications except the ephedrine and pentobarbital sodium. In addition, calcium gluconate and belladonna were prescribed. By the following day her eruption had cleared, and she returned to her usual job. A few minutes after she returned to work, her hands, arms and face "turned purple." This purplish discoloration, described by the foreman, disappeared within two to three hours before she returned to the dispensary. By noon her temperature was 102 F, and she was sent home. No eruption was apparent at the time. By the time she reached her private physician that afternoon her temperature was 103 F. She said he prescribed some tablets (one of the sulfonamides), which she took for two days. Within twenty-four hours after she began to take these she returned to work in the paymaster's office instead of on the trinitrotoluene production line. When next seen, on November 1, musical rales were still present in the chest, and she described asthmatic symptoms—wheezing, dyspnea and orthopnea. She was given 10 cc of a solution of theophylline ethylenediamine containing 0.24 Gm of the drug, intravenously, and a patch of trinitrotoluene was applied to her arm. This was done by dipping a one-half inch (1.27 cm) square of blotting paper in a saturated acetone solution of trinitrotoluene, allowing it to dry and affixing it under cellophane with adhesive tape. Within less than five minutes after the patch was applied she complained of itching on her chin and an urticarial eruption started at that site, extending downward to involve the entire body. The eruption faded out in fifteen to twenty minutes after an injection of epinephrine, 0.5 of a 1:1,000 solution, and immersion in a colloid bath. The patch was removed shortly after the urticaria appeared, and the site was cleansed with acetone.

The next day, 1 drop of trinitrotoluene in acetone solution was dropped on her arm and left uncovered. Four minutes later an urticarial eruption appeared on her chin. The trinitrotoluene was cleansed off immediately, and epinephrine was injected. The urticaria was not as extensive or severe as it had been the previous day when the trinitrotoluene had been left on longer. On both occasions, a macular erythema appeared within ten minutes at the sites of the trinitrotoluene patch tests,

reactions is found to decrease rapidly, and the serum always elicits negative reactions with the more sensitive (flocculation) tests and positive reactions with the less sensitive (complement fixation) tests. The need for verification tests shows that some of the modern technics are too sensitive. This is particularly true of flocculation tests, the result being that specificity is sacrificed for the attainment of greater sensitivity. More importance should be placed on the choice of suitable serum controls in routine diagnostic work.

HENSCHEL, Denver

**TREATMENT OF PEMPHIGUS** MAX WINKLER, *Dermatologica* **86** 209 (Oct-Nov) 1942

Four patients with pemphigus vulgaris were treated daily or once or twice weekly with intravenous or intramuscular injections of Germanin (suramin) ranging from 0.01 to 1 Gm. All 4 patients died, although in 1 case one course of Germanin seemed to have caused disappearance of the cutaneous lesions for a short while. In a questionable case of pemphigus vulgaris Germanin had only temporary effect.

**"TRICHOMALACIE"** (A HITHERTO UNKNOWN DISEASE OF THE SCALP) G. MIESCHER, *Dermatologica* **86** 227 (Oct-Nov) 1942

In a 5 year old child loss of hair was noticed eighteen months previously in two roundish areas, not sharply limited, near the vertex and on the occiput. These two spots improved with ultraviolet ray and local sulfur therapy, but a third spot developed.

The involved areas were at the time of this report about the size of a child's palm and irregular in outline. The center was almost without any hair, and at the periphery scanty hair or stumps, 1 to 2 mm long, remained. Most of the stumps were gray or colorless, deformed and thicker than the rest of the hair. Growing from the same follicle were apparently normal hairs, which, however, were easily pulled out or broke off. The follicles themselves either looked normal or appeared as hyperkeratotic elevated points resembling lichen pilaris. The scalp in these areas showed a mild degree of scaling and few pustular lesions not around the follicles. The whole area was slightly tender to touch. The rest of the hair, the nails and the skin of the body were normal. Laboratory examinations did not offer any clues.

Histologic examination showed that after fixation with Bouin's fluid either the whole hair or only the peripheral part did not take up the normal trinitrophenol stain. The shaft was not a rigid structure but wholly amorphous, blown up, curved and fissured. Bacteria but no fungi were demonstrated inside the hair. Five months later bacteria could not be demonstrated again, which was regarded as proof that they are only secondary invaders. The deformed hairs at that time showed dark brownish black pigmented lumps, which clinically gave the impression of black points in the follicles. The root of the hair showed disorganized matrix cells but no signs of inflammation.

The pathologic process consisted of disturbance of normal cornification and of formation of amorphous hair cylinders. It seemed to be of parasitic origin, but the causative agent had not been determined.

Therapeutically, roentgen rays, arsenicals internally and sulfur locally were beneficial. The disease, which was progressive in the beginning, had almost completely disappeared.

**POLYMORPHOUS DERMATOSIS DUE TO LIGHT** W. BURCKHARDT, *Dermatologica* **86** 249 (Oct-Nov) 1942

A 40 year old woman has suffered since the age of 36 from maximal sensitivity of the skin to light. Her sister may have a similar dermatosis. After only thirty minutes of exposure to the sun the skin of the exposed parts several hours later becomes itchy, red and swollen. Later papular lesions form, which subsequently start to ooze. No porphyrins were found. There was an eosinophil count of 16 per cent.

In experiments green and red light did not cause a reaction, while yellow light and ultraviolet rays of short and medium wavelengths produced the cutaneous lesions. Exposure to sunlight, even when filtered through window glass, was followed by swelling, redness and formation of papular lesions.

Histologically, some edema of the epidermis and perivascular infiltrations composed mainly of lymphocytes and a few leukocytes were seen in the cutis.

Daily injections of 0.1 cc of nicotinamide mitigated the sensitivity of the skin to light to such a degree that only after two hours of sunlight would a few papular lesions appear.

**HAND-SCHULLER-CHRISTIAN DISEASE WITH CUTANEOUS MANIFESTATIONS** W BURCKHARDT, *Dermatologica* **86**:250 (Oct-Nov) 1942

A 3 year old boy who had repeatedly suffered from otitis media showed at the age of 2½ years the triad of diabetes insipidus, protusio bulbi and typical defects of the skull. Pinhead-sized yellowish nodules covered with tiny scales together with purpuric petechiae were seen mostly on the chest. The scalp was covered with seborrheic-like scales.

The histologic picture showed subepidermal reticuloendothelioma without deposits of cholesterol.

Similar cases of reticuloendotheliosis with a more acute course were described under the name of Abt-Letterer-Siwe disease. Glanzmann and Walthard, who described such a case with similar cutaneous lesions, expressed the belief that this reticuloendotheliosis is an infectious disease sui generis and the deposits of cholesterol are secondary. In cases of the acute disease in children only few inner organs show deposits of cholesterol (Abt-Letterer-Siwe disease). Hand-Schuller-Christian disease with deposits of cholesterol develops only when remissions occur. Cases with similar cutaneous manifestations were reported by Gottron, Attig and Hofer.

**TROPHIC DISTURBANCES OF THE FINGER NAILS OF BOTH HANDS CAUSED BY FUNCTIONAL DISTURBANCES OF THE OVARIES** W STALDER, *Dermatologica* **86**:258 (Oct-Nov) 1942

A single woman of 24 noticed three years ago that one finger nail became brittle and that inflammation of the nail wall developed. Gradually all finger nails became involved. After a nail had crumbled, a new nail grew and remained normal for a while. Then the same cycle started again.

All examinations, including mycologic studies of the finger nails, showed normal conditions with the exception of hypoplasia of the genitals. The patient had started to menstruate at the age of 18, her menstruations were irregular and scanty. She was treated with injections of follicle-stimulating hormone after menstruation and corpus luteum hormone eight days before the menstruation. After four more recurrences the nails remained normal.

HELEN O. CURTH, New York

**PYODERMA IN INFECTED WOUNDS** P COLEMBIA and A KOSTAREV, *Sovet med* **10** 19 (Nov) 1943

In the pathogenesis of pyogenic infections of the skin an important factor is the presence of multiple minute breaks in the epidermis. These breaks constitute an invitation to pyogenic infection of the wounds.

There is a certain succession in the appearance of micro-organisms in the wounds. First, only anaerobes can be found, later, *Escherichia coli*, and after two or three weeks, streptococci and staphylococci. Consequently, the development of the pyogenic flora reaches its high peak not immediately after the wound is infected but after several weeks.

The authors introduced an ointment which they assert will prevent the invasion of pyogenic micro-organisms into wounds. The ointment, which acts as a prophylactic, consists of 3 per cent rectified oil of birch tar in equal parts of solution of calcium hydroxide and olive oil or any other vegetable oil. By repeating the procedure over one thousand times in over 200 cases, the authors verified the high efficacy of and good tolerance to this ointment.

GRADOW, San Francisco

# Society Transactions

## NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

HARRY C SAUNDERS, M D, *Chairman*

FRANK VERO, M D, *Secretary*

*Oct 3, 1944*

### A Case for Diagnosis (Fibroma, Neurofibroma?) Presented by Dr GEORGE M LEWIS

M M, a man aged 56, first noticed hard lumps in the midline of the upper part of the abdominal wall about three or four years ago. These remained fairly stationary until last year, when there was an obvious increase in size and a tendency to spread to adjacent areas. At present there are several hard nodules which are partly confluent, forming firm plaques 8 to 10 cm in width. The process involves the abdominal wall above the umbilical region. There is no tenderness and no other discomfort.

A specimen when sectioned was found to have a fairly normal epidermis, just beneath which was a tumor mass that involved sweat glands in interlacing bands of fibrous tissue alternating with cords of cells which stained pink with Masson's stain and had some resemblance to nerve trunks. The general appearance of the specimen indicated that it is a subcutaneous neurogenous fibroma. It is in no way malignant.

#### DISCUSSION

DR FRED WISE: Biopsy, of course, determines the nature of the tumor. The nerves are involved in the growth, but I do not think that one can call it a neurofibroma in the sense of von Recklinghausen's disease. I have always thought that a lesion like this should be called a fibroneuroma to distinguish it from neurofibromatosis.

DR FRANK COMBES: I agree with Dr Wise's statement that histologic study is necessary in order to arrive at a diagnosis, and I also agree that the patient's picture as a whole is not that of von Recklinghausen's disease. It was Dr Wise (Wise, F, and Eller, J J *J A M A* 86:86 [Jan 9] 1926) who wrote an article some years ago reviewing von Recklinghausen's disease and pointing out the diagnostic importance of the cafe-au-lait spots. This patient seems to have none, and I do not think that von Recklinghausen's disease exists without them.

DR EUGENE F TRAUB: Leaving the exact nature of this growth out of the discussion for a moment, I believe that a wide excision is the indicated method of treatment, in spite of the fact that the histologic structure suggests a non-malignant lesion, because the growth is multiple and there appear to be more nodules developing in the immediate area. If the lesion is not widely removed, the fact that new masses are developing in the general site of involvement would indicate that a recurrence might be anticipated.

DR ANTHONY C CIPOLLARO: Since the question of excising lesions of neurofibroma has come up, it is well to remember that Hosoi found that in 13 per cent of cases of von Recklinghausen's disease treated surgically sarcoma of the neurilemma developed.

DR GEORGE M LEWIS: The case interested me because of the localization of the tumors. Without a biopsy, one might hazard many diagnoses, without much

hope of settling the question. We do not think that it is one of von Recklinghausen's disease for there is nothing clinically to suggest that diagnosis, nevertheless, the histologic structure does show nerve trunks that seem to be part of the tumor. Dr. Foot, who has an international reputation for his work with such tumors, examined the sections, and his diagnosis was neurofibroma. I appreciate the suggestions as to therapy, particularly in regard to the potentialities for malignant degeneration.

### Cavernous Hemangioma with Ulceration Presented by DR. MARGARET M. KLUMPP

M. S., a woman aged 42, has had since birth a cavernous hemangioma involving the left leg, the pelvic regions and possibly the spleen, which is enlarged. The lesion has caused discomfort because of increasing size and weight, and the patient has been eager to submit to any procedure which might give promise of improvement. She was referred to various departments of the New York Hospital for opinions and therapeutic efforts, as follows:

1. Consideration was given to the repair of rectovaginal fistula, the result of packing which was necessitated by hemorrhage incurred during excision of an infected Bartholin gland in 1936. After surgical consultation it was decided not to attempt the procedure because of the great danger of hemorrhage.

2. Roentgenograms in 1937 showed no evidence of destructive or productive lesions of the skeleton. Films of soft tissue showed pronounced enlargement of the soft tissues of the left thigh and leg. The vascular channels on the left revealed clearly a hemangioma of the leg. The impression was that of "extensive cavernous hemangioma involving the entire left leg and thigh."

3. A series of high voltage roentgen ray treatments was given in March and again in June and September 1938. Drs. Carty and Tuggle felt that sufficient roentgen rays had been administered, with no improvement, and therefore treatment was discontinued.

4. Roentgen ray examination after injection of diodrast into vessels in 1937 and 1939 confirmed previous reports of the extent of the lesion throughout the entire leg and thigh, with no change during this period.

5. Two or three injections of a sclerosing agent into the veins near the left ankle resulted in a slightly firmer consistency just above the ankle and extending two thirds of the way to the knee.

At present the left leg is much larger than the right, with large purplish areas over most of the surface, composed of minute blood vessels and some larger tortuous blood vessels. The patient wears supportive elastic stockings. On the outer side of the left thigh is a quarter-sized eroded, crusted lesion which is the result of cauterization performed in June 1944 by a private physician in an attempt to stop hemorrhage in this region. The lesion has not healed, and the patient now comes for therapeutic suggestions.

### DISCUSSION

DR. EUGENE F. TRAUB: The area that has ulcerated should, in my opinion, be treated with the actual or cold cautery. The major portion of the lesion might be dealt with best by a compression bandage. For an adult with so extensive a lesion the only other type of treatment that could be considered would be the injection of a sclerosing material, and this might be a painful and long-drawn-out operation with only a fair chance for success.

DR. FRED WISE: I agree with Dr. Traub.

DR. FRANK C. COMBES: I presented this patient about 1925, and at that time, in addition to the hemangioma, she had morphea. Tonight she presents a new lesion of morphea on her right arm. I treated her for the morphea, and she got well—whether or not because of the treatment, I cannot say. As to Dr. Traub's remarks, I must have given the patient twenty or thirty injections of a

30 per cent solution of sodium salicylate for the angioma, and I succeeded in ridding her of the lesion around the ankle and back of the foot. Then I gave her the same sclerosing agent over the shin, ten or fifteen injections of good-sized doses, without any benefit whatever. I agree with Dr Traub that the granuloma pyogenicum could be curetted out.

This woman presents a real endocrine problem. She has little stellate telangiectases, which appear and disappear at the same time as the patches of morphea do. She formerly had intense headaches, and I sent her to an endocrinologist who gave her thyroid and pituitary.

DR FRANK VERO: This case brings up an interesting dermatologic problem—the early treatment of hemangiomas. Dermatologists are told by many pediatricians and physicians that hemangiomas should be left alone. This case illustrates the fact that there is little one can do when such patients are older. I should like to recall a case of massive angioma cavernosum which Dr Montgomery showed from the New York Polyclinic Medical School and Hospital before this Section last year (*ARCH DERMAT & SYPH* 48:670 [Dec] 1943) and in which the eruption was cured with solid carbon dioxide. In this case the right shoulder and arm were involved.

I believe that all patients with this disease should be treated in early infancy.

DR MARGARET M KLUMPP: Thank you for your suggestions, and I shall try to carry them out. I am especially interested in the additions to the history, which I did not know about. This case illustrates to me the futility of treatment of extensive lesions of this sort. Here is a case in which many of the suggestions which one hears at these meetings have been carried out, and, as far as I can see, the patient is not much better.

#### **Hemangioma Cavernosum Combined with Hemangiofibroma Tuberosum Multiplex Associated with Probable Involvement of the Right Optic and Acoustic Nerves** Presented by DR GEORGE M LEWIS

C P., a 61 year old Chinese laundryman, has had a new growth on the right side of the head since birth. He complains of poor vision in the right eye for the past eight years and deafness of the right ear for thirty years. Examination reveals an extensive cavernous hemangioma involving the right side of the neck, the right ear and the right temporal region. Within this area are several finger tip-sized cone-shaped, hemispherical doughy pendulous tumors. One of the latter was excised for histologic examination.

Sections from this small tumor revealed it to be composed of a number of widely dilated venous sinuses, scarcely enough to merit the term angioma but nevertheless constituting a tumor-like growth insofar as it consisted of large blood vessels in a fibrous stroma.

Roentgen ray examination of the teeth revealed that they were normal. Roentgen ray examination of the sinuses revealed definite clouding of the left sphenoid sinus.

From an ophthalmologic consultation the vision was reported to be 4/200 to 4/100 in the right eye and 20/70 to 20/30—3 in the left eye. The right eye showed a definite patch of what may be a juxtapapillary choroiditis. There was a tessellated fundus with some choroidal sclerosis.

Otolaryngologic consultation revealed 80 per cent deafness of the right ear and 35 per cent of the left. The frontal sinuses were normal to transillumination, but both maxillary sinuses illuminated poorly.

#### DISCUSSION

DR FREDERICK REISS (by invitation): The interesting feature in this case is the involvement of the optic and acoustic nerves. It is of course problematic whether there is a direct involvement or whether compression from the hemangioma is present. There is no doubt that the patient's hearing and vision are



impaired A further unusual feature is the mammillated tumors which are fibrous and which histologically show dilatations of vessels in a fibrous stroma On this basis one could classify the tumors as fibrohemangiomas

**Pustular Psoriasis Successfully Treated with Antimony and Potassium Tartrate** Presented by DR GEORGE M LEWIS

D S, a 47 year old white housewife, had a blister formation on the palms and soles about August 1942 This was followed two months later by a thickening of the affected areas which made walking uncomfortable Examination on Jan 14, 1943 revealed a heavy scale formation on the plantar aspect of all the toes, with considerable thickening of the nail plates, especially that of the big toe In the middle of the right sole there was a well demarcated erythematous area of the size of a small palm covered with heavy scales On the thenar eminences of both palms a similar process was present There were neurodermatitic patches on the right forearm and on the nape of the neck

Bacterial examination of blister contact of the hands and feet revealed *Staphylococcus aureus* Examination of the throat and teeth gave no evidence of focal infection Mycologic examination showed no fungi

Biopsy revealed pronounced parakeratosis, above which there was a scab composed of desquamated scales with small crusts of pus The epidermis was thickened, and the rete pegs formed a net of cords intertwining with one another The corium was thick and fibrous, and the inflammatory reaction in this was rather diffuse and made up of a variety of cells, among which polymorphonuclear leukocytes seemed to be numerous The inflammatory reaction in the corium was slight for acrodermatitis Plasma cells were not found in any considerable numbers There was no atrophy of the epidermis The blood vessels did not seem to be definitely inflamed, and there were no thrombi The process appeared to be as equivocal as the clinical signs The only indication of psoriasis was the pronounced parakeratosis which extended along the entire surface There were no "air spaces" The papillae did not approach the surface, as there was pronounced acanthosis which blocked such penetration of the epidermis

Treatment consisted in the administration of sulfapyridine and of roentgen rays and the local application of estrogenic hormones in ointment containing 10 per cent salicylic acid in petrolatum, all of which were of no avail On April 4 the administration of 1 per cent solution of antimony and potassium tartrate was begun, and after the fourth injection definite improvement was noticeable After the tenth injection thickening of the palms and soles had completely disappeared The right big toe nail is at present normal as to shape and thickness There was only a faint trace of scaliness, which was treated with local applications of cod liver oil Treatment was stopped in June, and the improved condition has remained unchanged since then

DISCUSSION

DR MAURICE J COSTELLO One of the patients presented by Dr Reiss I had cared for privately with the usual treatments roentgen rays and local therapy The last time she visited me she was better than she is tonight The other patient presented as successfully treated with this method, I think, has a number of lesions of pustular psoriasis on each heel now They may be greatly improved The characteristic of this disease is that the lesions clear up, recur, are persistent and are resistant to therapy

DR E WILLIAM ABRAMOWITZ Did Dr Reiss use antimony for psoriasis empirically or is there some pharmacologic basis for the use of the drug? Does he employ it for ordinary psoriasis or only for pustular psoriasis? My experience is that the latter disease is resistant to treatment Other metals, such as arsenic, bismuth and gold, have been employed in the treatment of psoriasis Some of the newer antimony compounds might be better tolerated and perhaps more efficacious

DR FRED WISE It is difficult to judge how much improvement this patient has shown because we did not see the original eruption I should like to have

Dr Reiss tell us more about that and about the distribution of the eruption elsewhere than on the palms and soles. It is desirable to try any remedy, even if it is empiric, as this one is, in pustular psoriasis because most treatments achieve no results or only temporary results or the eruption may even get worse from treatment with topical remedies and with such agents as arsenic, soybean lecithin and others. My intention is to try it out, to see what happens and to report the results.

DR GEORGE M LEWIS. I have seen 2 other patients that Dr Reiss has treated in the hospital, and those 2 also showed good results. While I am sure that Dr Reiss does not want to leave the impression that this is a certain cure for pustular psoriasis, his method would seem to be an addition to the therapy, which is otherwise none too good.

DR FREDERICK REISS (by invitation). This is meant simply to introduce a method which has helped in cases of recalcitrant pustular psoriasis. The patient was incapable of walking even a few steps because of the heavy scale formation on the heels. It is true that some lesions, which are probably dyshidrotic vesicles, are seen on the palms today, but, compared with the former eruption, they have practically regressed. The other patient has not been under treatment for the past five months, and there has not been the slightest relapse to date. I feel that psoriasis may be associated with a virus causation, and, since antimony has been used for many types of virus diseases, I thought that it might be beneficial in the treatment of psoriasis also. This treatment is not as effective for psoriasis vulgaris as for the pustular form. That the drug has some degree of specificity is shown by the fact that there is noticeable improvement in the eruption after three or four injections. I have been using topical applications also, such as cod liver oil.

I give 1 cc of antimony and potassium tartrate intravenously, gradually increasing the dose to 5 cc once a week.

#### **Tinea Capitis in a 2 Year Old Child** Presented by DR GEORGE M LEWIS

M S., a girl aged 2 years, was first seen at the New York Hospital on June 5, 1944. Her older sister had been sent home from school because of tinea capitis, and the patient was brought in as a contact. She has since received therapy with a penetrating ointment base containing diethylstilbestrol. There has been no demonstrable effect from this treatment.

Examination reveals typical patches of ringworm scattered over the scalp. *Microsporon audouinii* was demonstrated on culture.

Suggestions for therapy would be appreciated.

#### DISCUSSION

DR FRED WISE. I do not understand what Dr Lewis intended to emphasize in this case. Is it impossible to give roentgen rays to a 2 year old child? I think that a baby could be given an anesthetic, if necessary.

DR GEORGE M LEWIS. We have treated several preschool children with roentgen rays, and it is surprising how children even 3 or 4 years old will cooperate. There is more difficulty with children as young as 2 years, and I am not sure that they should be so treated. I am interested in the fact that no one mentioned any form of therapy other than roentgen irradiation. We thought that some other treatment might be advisable, and therefore Dr Reiss gave the patient diethylstilbestrol by local application. In a small series of cases in which the patients were similarly treated, we were disappointed in the results.

DR EMANUEL MUSKATBLIT. In the New York University dermatologic clinic roentgen rays are not given to children below the age of 4 years. It is almost impossible to keep small children quiet for two and one-half minutes in each of five positions. They begin to talk and move, and the roentgenologist has to stop.

It is possible to do it with an anesthetic. I recall that in Russia some children were given enemas of chloral hydrate and while the child was asleep the head could be fixed with blocks or sandbags and treatment administered.

Roentgen epilation of small children may be dangerous because of the small size of their heads. One risks overlapping of rays. It may be difficult to mark the five points with correct distances between them on a small head. Another point which has been stressed is that small children have tender bones, as ossification has not been completed, and that radiation may reach the meninges and even the brain and cause trouble in later years. This danger is more imaginary than real.

If one is conservative and refuses to treat a 2 year old child with roentgen rays and if the infection is due to *M. audouini*, the parents must be told to wait two or three years before the treatment can be given. Although these young children do not lose school, the situation is still not an easy one.

DR ANTHONY C CIPOLLARO. I should like to see stricken from the record the remark that roentgen rays as used by dermatologists in the treatment of *tinea capitis* may damage the brain. There is no scientific basis for such a statement. Most children of 2 or 3 years of age can be treated with roentgen rays from a shock-proof apparatus, the four point method being used.

DR EUGENE F TRAUB. The age of the patient does not seem to me to be a contraindication for treatment with roentgen rays. In the ten or fifteen years following 1920, while I was responsible for the roentgen ray therapy at the New York Skin and Cancer Hospital, we never hesitated to epilate a child regardless of its age. The youngest patients were tightly wrapped in a sheet or blanket so that they could not move, and the head, properly protected, was held in place by the parents or an attendant. An anesthetic was never necessary. We also tried partial epilation, which was successful in a number of cases. If in those days we had followed up our patients with the Wood light or had examined them with this light prior to treatment, our percentage of success with the localized method of treatment might have been greater. However, I trust that no one has implied that the five point method is invariably successful, because I can assure you that this is not the case, regardless of the operator.

DR CHARLES LERNER. I can readily understand Dr Lewis' predicament in this case. I should prefer to treat the scalp of this child with antiparasitic ointments. Anesthetizing so young a child, especially in a roentgen therapy room, is a difficult and cumbersome task, and I do not think that it is practical. The difficulty that one encounters in trying to epilate so young a child can often be overcome by rehearsing the epilation procedure without turning on the rays. By gradually overcoming apprehension the child can finally be trained to stay quiet. Personally, I always hesitate to epilate the scalp of a child under 6 years of age.

DR GEORGE M LEWIS. I am glad to have Dr Cipollaro's suggestion of the four point method, which should be workable with a small head. I think that the circumference of the head may be more important than the age of the patient.

#### **Dermatitis Medicamentosa (Probably Due to Phenolphthalein). Presented by DR MARGARET M KLUMPP**

R C, a girl aged 13, is presented from the New York Hospital, with a bullous eruption of the legs. About September 22, bullae first appeared on the lower third of each leg. About five days before that, the patient took a teaspoonful of a laxative, the nature of which is unknown as the bottle was thrown away. There is moderate pruritus. There is no history of the patient's going to the country.

In July 1943, blisters similar in appearance to the present eruption appeared on the right thigh and left ankle. Again there was no history of a trip to the country. The patient states that she has similar attacks each summer.

Large pea-sized bullae with a noninflammatory base are distributed symmetrically over the lower third of each leg. No scarring from previous attacks is seen.

Biopsy revealed a ruptured and superficial bulla in an area of skin entirely flattened out and devoid of rete pegs. There was a dense infiltrate about the vessels of the corium, consisting of polymorphonuclear leukocytes, which invaded the basal layer of the epidermis in some places. The deeper layer of this structure showed some necrosis. The picture was felt to be characteristic of a drug eruption.

#### DISCUSSION

DR E. WILLIAM ABRAMOWITZ: This may be a drug eruption, but I do not think that it is due to phenolphthalein, and it is not a fixed eruption, even though it is said to recur in the same areas. When a drug eruption is severe enough to produce bullae, it also causes a red areola and is followed by pigmentation. The patient takes some syrup each summer. A test dose should be given to see whether the eruption returns. I think that it is a bullous type of erythema that may be due to a number of causes.

DR CHARLES A. GREENHOUSE: I suggest a diagnosis of pemphigus virginum. This occurs in young females, recurs from time to time in crops of large vesicles and bullae and persists for several weeks. I believe that the patient presented tonight has a disease that fits well into this category.

DR. EUGENE T. BERNSTEIN: The interesting feature in this case is that the eruption recurs every summer. I questioned the child, and she said that in the summer she does not wear socks. I suggest the simple diagnosis of hydroa estivale. This is a bullous eruption which recurs every summer on exposure to sun and heat.

DR. JESSE A. TOLMACH: I do not think that the eruption should be called pemphigus virginum, because I now have as a patient a young boy who has had the same type of eruption for two successive summers.

DR. FRED WISE: In a large clinic my colleagues and I see perhaps not more than 2 cases in a year exactly like this one, with tense bullae on the lower extremities, and I have always considered them to be unclassified. I questioned this girl closely about contact with plants, and the answers were negative. The results of patch tests were negative. Naturally one always thinks of some endocrine disorder. Pemphigus virginum is a farfetched diagnosis for a patient otherwise healthy. I should like to hear the opinion of others regarding such eruptions.

DR. MAX SCHEER: In this case there are bullae which show no inflammatory halo but which seem to arise on normal skin. I was wondering whether these cases cannot be classified in the group of cases of epidermolysis bullosa. Most patients give a familial history, but some do not, and I suggest that as a diagnosis for consideration.

DR. EUGENE F. TRAUB: It is possible that this eruption might be caused by insect bites, although I could not get that history in this case. I have seen a number of similar cases, however, particularly on Long Island, in which bullous lesions on the lower extremities were caused by flea bites.

DR. MARGARET M. KLUMPP: As regards hydroa estivale, this eruption appeared late in summer—about September—and the patient had not at that time been exposed to the sun, although she had been so exposed all summer without ill effect. I think that that fact practically rules out hydroa estivale. This eruption appeared one year ago, I saw the patient in July 1943, when there were blisters in the same location as there are tonight and, in addition to this, on the covered parts of the right thigh. At that time a diagnosis of dermatitis venenata was made, and the patient was then lost to observation. I think that the possibility of insect bites could be ruled out. There was no inflammation, and the blisters were tense, large and superficial. Tonight there is a slight halo around

the periphery of these blisters, but it was not there in the beginning, and there is no itching. I am not at all sure that the eruption is dermatitis medicamentosa. It is known that five days before the appearance of the eruption the patient took a laxative, but the bottle has been thrown away.

### Triple Symptom Complex of Behcet Presented by DR HELEN O CURTH

(This patient was previously presented, Oct 5, 1943, with a diagnosis of post-operative anophthalmos of the left eye, uveitis and choroiditis of the right eye, possibly due to the virus of lymphogranuloma venereum.)

J T, a white man aged 24, of Italian parentage, has had no further attacks of iritis since the last presentation. The vision of the remaining eye, however, has become very poor. The patient has suffered from recurrent attacks of small ulcers in the mouth, which he has experienced on and off for many years. In August of this year the patient was seen with several pinpoint aphthous lesions of the buccal mucosa. He had several attacks of large genital sores. When seen in August and September he had large dirty-looking ulcerations on the right side of the scrotum without inguinal adenitis. The patient was admitted to the Institute of Ophthalmology of the Presbyterian Hospital in the city of New York a week ago for a course of penicillin treatments and has today completed a course of 2,400,000 units. The genital lesions practically healed within four days, and the vision has subjectively improved slightly. While he was receiving penicillin, a large boil developed on his back and there was inflammation at the sites of many injections of penicillin on the buttocks. The temperature, which at that time rose to 101 F, is normal now.

Examination reveals postoperative anophthalmos of the left eye and uveitis and choroiditis of the right eye. The mouth is free of lesions. A scar is seen on the left part of the lower lip. There are some old scars on the scrotum, and a crust is left on a small lesion on the right side of the scrotum. There is a mild inguinal adenitis on the left side due to inflammation of the left buttock at the site of an injection of penicillin.

Laboratory examinations. Tests with Frei antigen-dmelcos and isotonic solution of sodium chloride by injections were repeated, eliciting the following reactions: Frei test (on left arm, Sept 27, 1944), positive, Ducrey test (on right arm Sept 27, 1944), strongly positive, and a control test with saline solution (on right forearm, Sept 29, 1944), negative.

NOTE—At one time last year the control test with saline solution had elicited an uncharacteristic redness of the injection site.

### DISCUSSION

DR HELEN O CURTH. This case was presented again tonight because I felt that it shows the fully developed picture of Behcet's triple symptom complex. Although nothing is known about the causation, the conception of the syndrome may help one to recognize what the disease is not. This patient has no venereal disease—at least, what he presents tonight cannot be explained on the basis of venereal disease. Last year the patient was shown with a diagnosis of lymphogranuloma venereum, and the lesions were considered to be chancroids on clinical grounds. It would be rather unusual in cases of chancroids to see recurrent lesions on the genitals where Ducrey's bacilli could not be found and with no involvement of the inguinal lymph nodes. Recognizing the syndrome, one also learns something of the bad prognosis. In all these cases the second eye invariably becomes involved, and the disease ends with complete blindness. Thirdly, many patients with one symptom missing may have Behcet's syndrome, because all three manifestations (eye, mouth and genitals) may not occur simultaneously or alternately and it may take many years before the third manifestation becomes apparent. In women the genital lesion is often described as *ulcus vulvae acutum*. It often occurs together with aphthous lesions of the mouth.

With regard to the question of lymphogranuloma venereum, this patient gives a history of bubo many years ago, and the Frei test elicited a positive reaction.

A test with saline solution elicited a negative reaction while the patient was being treated with penicillin. Before receiving penicillin, he once showed uncharacteristic redness to a test with saline solution. In the literature many authors report that these patients have such a sensitivity to intradermal tests that they react positively to all or even to the prick of a needle. Our patient reacted negatively to high dilutions of tuberculin.

I tried penicillin for obvious reasons. Other medications recommended are the sulfonamide drugs and vitamin B. The patient is of Italian parentage. He has a large vegetable garden, and his diet seems adequate.

#### **A Case for Diagnosis (Tattoo, Postinflammatory Hyperpigmentation?)**

Presented by DR. GEORGE M. LEWIS

C. F., a woman aged 39, is presented from the New York Hospital. She was first examined on July 17, 1944, stating that five weeks previously she submitted to an electrical treatment in the office of a former European midwife, who was now said to be a licensed electrologist. She had formerly undergone a series of eighty-five treatments with electrolysis in the office of a dermatologist and several treatments of multiple needle electrolysis at the hands of the former midwife, without any undue reaction or unwanted sequelae. She is now concerned over the appearance of the skin.

There are some residual focal pigmentation and pitting of the skin of the cheeks. This pigmentation has become less pronounced during the two and a half months since she was first observed.

#### DISCUSSION

DR. MAURICE J. COSTELLO: The hyperpigmentation and pitted scarring which this patient presents are the types of lesions which follow inept attempts to remove hair with the short wave high frequency current. I believe that this method was employed for this patient, because she said a rapid instantaneous "spark" had been used. This is another example of the evasion of the Medical Practice Act by lay practitioners. Under the law I do not think that this group has any right to employ the high frequency current for the removal of superfluous hair.

DR. GEORGE M. LEWIS: There has been considerable improvement in the condition of this patient. When she was first examined, the pigmentation impressed me as electrolytic tattoo from the use of the positive pole instead of the negative. However, there has been a gradual disappearance of the pigment, hence, I now believe that the depressed and hyperpigmented areas have been caused by some form of electrodesiccation.

#### **Telangiectasia of Tip of Nose (Rosacea, Lupus Erythematosus?)**

Presented by DR. MABEL G. SILVERBERG

M. G., a man aged 56, has noticed redness of the tip of the nose for the past fifteen months. Three years ago he sustained a fracture of the left orbit, followed by operative repair. Since coming to the clinic the patient has received only light applications of solid carbon dioxide.

The middle third of the nose is bright red, shiny and oily. The boundaries of the lesions are sharp and resemble a rough square. On close inspection the lesions show telangiectasia.

The Mazzini test elicited a negative reaction on March 4, 1944.

Biopsy performed in June revealed an acute inflammation of the basal layer of the epidermis which showed an increase in sebaceous glands and numerous hair follicles which did not exhibit much inflammation. The corium was fairly dense and showed broken-up elastic fibers scattered throughout and in some places almost resembling fibrin. They seemed to be fragmented. There were mantles

of lymphocytes about the vessels of the cutis, and the latter were congested with blood. The picture was fairly typical of a rather acute phase of rosacea without, however, exhibiting any of the acneform lesions.

## DISCUSSION

DR EUGENE F. TRAUB: Inspecting this patient on one occasion, I was impressed at once by the sharp demarcation of the telangiectatic eruption. There was also some suggestion of pigmentation and atrophy. The entire picture is compatible with sequelae of irradiation. On being questioned, the patient stated that he had treatments with roentgen rays on several occasions, one for work done on his lower teeth and the others for something in connection with the left eye. It is possible, therefore, that portions of this eruption, if not the entire picture, represent sequelae of irradiation.

DR FRANK C. COMBES: I agree entirely with Dr. Traub's diagnosis.

DR MARGARET M. KLUMPP: The patient had a fracture of the orbit, and I am sure that roentgenologic studies were made at that time.

DR FREDERICK REISS (by invitation): I examined the sections in this case and they certainly do not give evidence of damage from radiation. They reveal hyperplasia and increase of the sebaceous glands, without any sign of atrophy of the skin and its appendages.

DR MARGARET M. KLUMPP: The dilated blood vessels were so sharply defined that the lesion looked almost like a nevus. The patient was given weekly treatments with solid carbon dioxide until I was satisfied that there had been absolutely no change, hence, I am still at a loss.

DR E. WILLIAM ABRAMOWITZ: At the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital several patients have been seen with telangiectasia and redness of a limited area at the tip of the nose. I believe that they have some chronic infectious process of the maxillary sinuses as an underlying cause.

DR MAURICE J. COSTELLO: I agree with Dr. Wise and believe that the eruption is a manifestation of rosacea. Long telangiectases which are parallel to the long axis of the nose, without any other sign of radiodermatitis, militate against the latter diagnosis. I suggest that these blood vessels be destroyed with the electric needle.

DR GEORGE M. LEWIS: Although sequelae due to roentgen rays were considered in the differential diagnosis, the absence of atrophy and hyperpigmentation and the histologic changes rule out such a possibility. We also thought of lupus erythematosus of the telangiectatic type, but we feel that the location, clinical appearance and age of the patient favor rosacea.

#### A Case for Diagnosis (Hemangioendothelioma, Hemangiofibroma?)

Presented by DR. GEORGE M. LEWIS

A O., a 69 year old white housewife, thirteen years ago noticed under the left lower eyelid a hardly perceptible red nodule. This remained stationary until six months ago, when there was a sudden increase in growth. The lesion has now reached a spheroid shape,  $\frac{1}{2}$  inch (1.27 cm) in diameter, and bleeds freely at times.

In the center under the left lower eyelid is an encapsulated, freely movable, painless tumor. The lesion has a rubbery consistency and a reddish-bluish color. There is no fluctuation. In addition there are several soft fibromas and hairy nevi on the right side of the face, on the neck and on the chest.

## DISCUSSION

DR. FRED WISE: The lesion is tense, globular and easily movable, as though it were some kind of cyst rather than a solid tumor. I think that it is not an endothelioma.

DR EUGENE F TRAUB This lesion is a hydrocystoma. If Dr Lewis will puncture it with a needle, I am sure that watery fluid will be obtained, and if the lesion is completely collapsed the sweat ducts will again fill it up.

DR CHARLES LERNER I think that the patient had traumatized the lesion. She said that she had tried to draw something out of it.

DR E WILLIAM ABRAMOWITZ I think that it would be a good idea to aspirate the lesion.

DR FREDERICK REISS (by invitation) There is some degree of softness in the tumor, but I do not see any evidence of cyst formation. There is a doughy feeling, and the recent increase in size is indicative, or at least suggestive, of a new growth.

### **Lupus Erythematosus of the Eyelids, Chest and Neck Presented by DR MARGARET M KLUMPP**

E. B., a woman aged 28, is presented from the New York Hospital with an eruption on the eyelids, on the upper part of the chest and on the neck, which has been present for six years. She is presented for therapeutic suggestions.

About 1938, when the patient was 22, patches first developed on the eyelids and the neck. The following year she had her first pregnancy, during which the cutaneous lesions disappeared. In 1940 the eruption recurred and, according to biopsy at the New York Skin and Cancer Hospital, a supraclavicular lesion was diagnosed as a toxic dermatitis.

The patient then attended the New York Hospital where she received twenty-five injections of 1.5 cc each of bismuth subsalicylate in oil (0.13 Gm of the drug) weekly, from 1940 to 1941. From April to December 1941, twenty-four injections of gold sodium thiosulfate were administered, the dose varying from 10 to 50 mg. No further treatment was given at the time as another pregnancy occurred with miscarriage in November 1941. The patient was not seen again until July 1943, and from then until November, when she received eighteen injections of a gold preparation. From November to April 1944, she was given eleven injections of liver extract and injections of catarrh vaccine and vitamins by mouth. From April to August, seventeen injections of oxophenarsine hydrochloride were administered, beginning with 0.005 mg, each dose being increased by 0.005 mg until 0.04 mg was being given.

The third pregnancy occurred in 1942 and went to full term. The lesions again cleared during this pregnancy.

Physical examination reveals coarctation of the aorta, probably congenital. This was accompanied with hypertension, especially during pregnancy and in later years. There is no evidence of other systemic disease.

Typical patches of lupus erythematosus, some with atrophy and some with edema, telangiectasia and crusting, are present on the eyelids, chest and neck.

Repeated urinalyses have shown no abnormalities. The blood count showed the size and shape of the red blood cells to be normal. The white cell count was 7,650, with 53 per cent lymphocytes, 40 per cent polymorphonuclear leukocytes, 2 per cent monocytes, 2 per cent band forms and 3 per cent eosinophils. Red blood cells numbered 4,300,000, the volume was 40 per cent, and the sedimentation rate had a total fall of 1 mg per hour.

### **DISCUSSION**

DR E WILLIAM ABRAMOWITZ I suggest that a different type of gold compound, such as triphal, be tried. Transfusions of blood at prolonged intervals may also help to build up resistance.

DR FRED WISF Am I correct in my assumption that if one form of gold compound is not successful others should be tried? Specialists in the treatment of arthritis use half a dozen varieties of gold. Dr Traub has had successful results in the treatment of lupus erythematosus with vaccines. I think that those two methods of treatment should be given a thorough trial, combined with adjuvant therapy with solid carbon dioxide.



DR MARGARET M KLUMPP I am grateful for any suggestions because the patient has received catarrh vaccine, gold compound, liver extract and oxophenarsine hydrochloride without benefit

### LOS ANGELES DERMATOLOGICAL SOCIETY

A FLETCHER HALL, M D, *Chairman*

CLEMENT E COUNTER, M D, *Secretary*

*Oct 10, 1944*

#### Congenital Fistula Presented by DR JOHN D ROGERS

When R D, a girl aged 12 years, was born, her mother noticed two small openings or dimples at corresponding locations on the external ears. No swelling was present until the child was 3 years old. Then a lesion similar to a boil appeared about 0.5 cm anterior to the dimple-like opening on the right ear. The lesion appeared to the physician to be a wen, and he incised it and evacuated cheeselike material. The lesion healed and remained well until the child was 5 years old. Since then she has had similar swellings three times. The first two swellings healed after being drained, but since the third swelling occurred, two years ago, the lesion has drained continuously. The father had similar sinuses in the same location, but he has never had any trouble. She has one sister, and that sister has no similar deformity.

Just anterior to the right tragus is a cicatricial lesion covered with a crust, about 1.5 cm in diameter. There appears to be a fistulous opening leading from this lesion to an opening on the crus of the helix. Purulent material exudes from this opening. The left ear has a similar opening without swelling or drainage.

#### DISCUSSION

DR HAL E FREEMAN I believe that these lesions are branchial cleft cysts developing from an embryologic fault.

DR H C L LINDSAY They are congenital openings on both ears. In the old days they used to be called accessory auditory meatuses. It is possible that the inflamed area has been infected by tuberculosis.

DR NELSON PAUL ANDERSON This case represents a classic example of a congenital preauricular fistula. If one examines both ears, one will find a small pit at the ascending ramus of the helix in front of each ear. This anomaly occurs often in families and is inherited to a decided degree. I know of one family in which it was traced back for seven generations. The particular granulomatous lesion now present in front of the ear is connected definitely with a small pit on the ascending ramus of the helix. To cure the anomaly one must take a probe or other instrument, insert it in the small opening, run it down to the granulomatous lesion, cut the fistulous tract wide open and destroy the epithelial lining. Almost all such patients presented before dermatologic societies or surgical societies give the same history of previous operations with recurrences. The granulomatous lesion will never disappear until that fistulous tract is destroyed. Dr Samuel Becker, some years ago, had 2 cases which unfortunately were published not in the ARCHIVES but elsewhere. The only case recognized and published recently in a dermatologic journal was the one by Dr F T Becker, of Duluth.

DR PAUL FOSTER I had a patient about four months ago with a similar condition. I missed the diagnosis at first because she had been operated on. Later, it was confirmed that she had an auricular opening. I was foolish enough to think that I could cause it to heal by the introduction of escharotic substances into the opening. I do not believe that this can be done.

DR CLEMENT COUNTER My experience with 1 patient reveals the difficulty of opening such a sinus tract. The operation was performed by an excellent otolaryngologist, and a paralysis of the lower right side of the face resulted. It is easy to injure the facial nerve by the surgical treatment necessary to cure such a sinus.

**A Case for Diagnosis (Sarcoid?)** Presented by DR NELSON PAUL ANDERSON

E M, a white woman aged 65, had an operation at New York Hospital for the removal of a blind abscess on the anterior surface of the neck, one year ago. A small amount of pus was evacuated.

Now there is a depressed scar on the right side of the neck anterior to the sternocleidomastoid muscle. There is also an atrophic scarred area on the bridge of the nose following radium treatment at Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York City. On the lateral surface of the right foot there is a tumor about 3 cm in diameter, and a similar subcutaneous lesion is on the right side.

The Wassermann reaction of the blood was negative. The roentgenologic examination of the long bones showed no lesions.

DISCUSSION

DR M E OBERMAYER It is possible that histologic examination will show the picture of lupus pernio rather than that of sarcoid. The location and clinical appearance of the lesions as well as the presence of "chilblain circulation" are suggestive.

DR NELSON PAUL ANDERSON I really have not the slightest idea of the correct diagnosis, and I believe that microscopic examination will be necessary before a definite conclusion can be reached.

**Pigmented Nevus** Presented by DR IRVING R BANCROFT

D W, a Chinese girl aged 4 years, presents an oval brown-pigmented slightly raised, papular lesion on the left side of the forehead 2 cm in its longest diameter. The surface is soft, fine textured and covered with fine dark brown hairs. It has increased to its present size from a greatest diameter of 6 mm when observed at birth. There has never been any inflammation. A similar but smaller nevus is located on the medial side of the left leg. The lesion on the leg has not increased in size. The case is presented for a discussion of the appropriate treatment.

DISCUSSION

DR KENNETH STOUT I should like to ask whether any one has observed a hairy pigmented nevus which has become malignant. I understand that such lesions do not become malignant.

DR H C L LINDSAY I had a patient with numerous hairy moles. One became malignant. Metastasis had possibly taken place before this mole was taken off. It was treated by radium under the direction of Dr George Sharpe. The child ultimately died.

DR A FLETCHER HALL May I ask whether it was ordinary hair or lanugo hair?

DR H C L LINDSAY The main lesion on the arm was covered with long hair, monkey-like hair. Other moles on the body covered about one sixteenth of the body surface, most of them were hairy.

DR M E OBERMAYER The lesion is a simple nevus pigmentosus et pilosus, and if it is excised excision is for cosmetic purposes only. I think that there is no indication for immediate operation, and I wonder whether the reported rapid growth of the nevus is not relative and in keeping with the growth of the body.

DR HAL E FREEMAN Why would it not be better to excise it now, when the child is younger, than to wait until a later date? It seems to me the earlier the better for cosmetic results

DR IRVING R BANCROFT I did not know whether it should be removed with solid carbon dioxide or whether it should be excised I think that the lesion has increased in size far out of proportion to the general increase in size of the child

**A Case for Diagnosis (Rosacea?) Presented by DR A FLETCHER HALL**

K H P is a 26 year old married white American housewife Her first eruption began in January 1943, when a redness developed on the lower part of her face, with numerous tiny pustules This cleared after two roentgen ray treatments, given by another physician, and the elimination of foods to which she had positive reactions to scratch tests The face remained clear for several months, but redness recurred during the summer of 1943 Tiny pustules were also present again The eruption has continued since then without change regardless of treatment Numerous new pustules appear every morning

The chin, the folds at the sides of the mouth, the nasolabial folds and the nose are involved in a continuous patch of redness Numerous follicular openings are occupied by tiny sessile pustules, while sites of ruptured pustules are marked by crusts The redness is due to erythema rather than to telangiectasia Diascopic examination reveals no residual pigmentation

The following treatment has been used without benefit One roentgen ray treatment of 60 r was given ten months ago An ointment containing 3 per cent each of salicylic acid and sulfur and 5 per cent of juniper tar was applied to the scalp and face This caused irritation, and its use was discontinued Later, sulfathiazole ointment was used together with boric acid compresses, which reduced pustule formation while it was used Four U S P units of crude liver extract with 100 mg of thiamine hydrochloride was given intramuscularly twice weekly for eighteen weeks Intravenously, gold sodium thiosulfate was given in doses up to 50 mg once weekly for six doses Smallpox vaccination was performed daily for five days Staphylococcus toxoid was injected five times in two weeks There has been no treatment for one month

DISCUSSION

DR W H GOECKERMAN In the absence of biopsy I favor the diagnosis of rosacea I think that the appearance fits that diagnosis Rosacea manifests itself in different clinical appearances

DR SAMUEL AYRES JR The lesion was unique I have never seen one exactly like it The peculiar suboral distribution suggests features of seborrheic dermatitis I think that sulfur and salicylic acid ointment would be helpful

DR A FLETCHER HALL The patient has used an ointment of salicylic acid, sulfur and juniper tar for the face and scalp It produced no benefit but was irritating She may have been sensitive to one of the ingredients

DR M E OBERMAYER Dr Goeckerman's suggestion is undoubtedly correct Though it is unusual to see such sharply bordered lesions in rosacea, the presence of erythema and pustules on the forehead, the red nose, the seborrheic background and the age of the woman are all in support of the diagnosis of rosacea

DR PAUL FOSTER This is an unusual type of circumoral eruption strongly suggesting rosacea In view of the fact that she has not had a gastric analysis, I suggest either that she have a gastric analysis made or that she be given rather large doses of dilute hydrochloric acid by mouth as a therapeutic test

DR A FLETCHER HALL This was first considered to be a possible seborrheic dermatitis, and then the thought that it might be a reaction to roentgen rays occurred At that time only the redness was present, with no pustules It was so well circumscribed and so constant in its character that an overdose of roentgen

ray treatment was suspected. When the pustules appeared, that idea was given up. A rosacea was not considered earlier because of the constant limits of the eruption and the confluent character of the eruption.

**Arsenical Keratoses Disappearing with Vitamin A Therapy** Presented by  
DR A FLETCHER HALL

H M, a 39 year old white man, is an automobile mechanic. No members of his family are known to have had cutaneous abnormalities of the palms and soles.

From the age of 7 to 13, he took solution of potassium arsenite for the treatment of chorea. About seven years after he quit taking that drug the first warty lesions occurred on the palms. Similar lesions have appeared since then on the soles. Some have been removed as papillomas. During the past twenty years the warty lesions have increased in number, size and thickness. Pale patches on the backs of the hands were noted four months ago. Three months ago the palmar aspects of the hands and the fingers were studded with numerous yellowish to yellowish orange thickenings varying in size from that of a small pinhead to that of a large pea. Many of these lesions showed depressed centers. The palmar aspect of the web between the left second and third fingers was the site of a large, pea-sized, abruptly elevated keratosis, with a deep fissure at each side. There were practically no uninvolved areas on the palms. The soles showed numerous tiny, pinhead-sized, comparatively superficial keratoses. The dorsal aspects of both hands and wrists showed numerous well defined, milky white, depigmented macules varying in size from that of a pinhead to that of a pea.

After three months of ingestion of vitamin A, 150,000 U S P units daily, there are many uninvolved areas on the palms. The warty lesions are much fewer. The lesions which are still present on the average are smaller. The areas of depigmentation have disappeared from the backs of the hands and wrists. Ten per cent boric acid ointment containing 6 per cent salicylic acid has been used locally.

DISCUSSION

DR W H GOECKERMAN: I have treated a number of patients like this one, and most of them have done remarkably well. Vitamin A must be given in large doses over a long period. I have repeatedly emphasized that I do not think that one should talk longer about avitaminosis, hypovitaminosis or dysvitaminosis in cases of this kind. Vitamin A does something to the skin, which is not fully understood. It acts in a pharmacologic or biochemical manner in various types of dyskeratosis. It is likely that its effect is brought about in an indirect manner, possibly because of some effect on the liver or gonads. I suspect that it does this by producing some new chemical. This is suspected because smaller physiologic doses are of no value in such cases, and the vitamin must be given over a considerable time. I have some evidence that in large doses it has a considerable effect on the entire ectodermal system. What can be done occasionally for these dyskeratotic conditions surprises every one.

DR NELSON PAUL ANDERSON: How much improvement do you think there is?

DR A FLETCHER HALL: To say how much improvement there is, one would have to define the basis for starting and ending. All I can say is that there was not a normal area on the patient's palms large enough to put the butt end of a pencil on before treatment was started three months ago. There are now irregular dime-sized clear areas on the hypothenar eminences and on the pads at the bases of the index fingers and elsewhere. Lesions that remain average about half of their original size. The large lesion on the web between the left index and third fingers which I strongly suspected was malignant when I first saw the patient I am in no hurry to excise, because it does not appear to be malignant now. If vitamin A will reverse the process started by arsenic in the palms and soles, it may be possible for it to reverse a malignant process. The pigmentary changes which were present on the dorsa of the hands and wrists when I first saw the patient disappeared within the first two months of treatment.

**A. Case for Diagnosis (Late Syphilis)** Presented by DR SAMUEL AYRES JR.

E G, a white man aged 57, was presented before the Los Angeles Dermatological Society previously, on Oct 12, 1943 and on Feb 8, 1944

The original ulcer began on the left leg May 17, 1942 The patient was hospitalized three months later Two weeks after he entered the hospital numerous smaller ulcers began The first lesion resulted from bumping his shin against a desk Ulcers have been present ever since, always confined to the legs and thighs On two previous occasions the lesions cleared about 95 per cent while he was hospitalized The first improvement came after the use of wet dressings of Alibour water (water containing zinc and copper sulfates) and of solutions of gentian violet medicinal and the application of chlorohydroxyquinoline ointment The second improvement came while he was using wet compresses of boric acid and receiving injections of penicillin His eruption relapsed each time after he left the hospital He has received a great variety of treatment, including oxophenarsine hydrochloride, a bismuth compound, twenty-five injections of Fuadin, autogenous vaccine containing a mixture of staphylococci and streptococci, over two million units of penicillin and such local applications as Alibour water, solution of gentian violet medicinal, chlorohydroxyquinoline ointment, paste of zinc oxide, wet compresses of tyrothricin, wet compresses of acriflavine, solution 1 1,000 neutral and sulfadiazine ointment Sulfadiazine was also given orally in adequate dosage for eight days, without benefit The patient has now been hospitalized for the past ten days and has shown considerable improvement following the use of nothing but wet compresses of saturated solution of boric acid

Scattered over the legs and thighs are a dozen ulcers Some are dime sized, and others are hand sized Many lesions are kidney shaped, with sloping granulating edges and a bright red granulating base There is an erythematous halo around the active margins of the ulcers Kidney-shaped ulcers usually have an elevation of the convex margin There are numerous soft white pigmented scars of previous ulcers now healed

The Wassermann, Kahn and Kline reactions of the blood have been negative repeatedly The Eagle reaction was negative once, and the Hinton reaction was positive once The urine has been normal except for an occasional trace of albumin. Stained smears contained no Donovan bodies Various bacteria have been present The most recent culture had *Bacillus pyocyaneus*, *Staphylococcus albus* and a streptococcus Tests of the blood bromides one year ago and one month ago gave negative results

A report on the biopsy described a chronic inflammatory process suggestive of an eruption due to an iodide The patient has repeatedly said that he had not used bromides or iodides His wife states that when he is at home he spends two or three hours at a time dressing his lesions

## DISCUSSION

DR HAL E FREEMAN These lesions which have piled-up borders and undermined edges are not typical but are strongly suggestive of the burrowing ulcers originally described by Meleney These respond more or less to zinc peroxide medicinal if it is properly activated I should like to make that therapeutic suggestion in this case Such burrowing ulcers are caused by a hemolytic streptococcus

DR PAUL FOSTER I do not remember the discussion which took place when this patient was presented at a previous date, but I think that one cannot completely eliminate the possibility of a dermatitis factitia in conjunction with something else The fact that the patient spends hours dressing the lesions would seem to indicate that possibly he produces some of them himself

DR SAMUEL AYRES JR I doubt that this type of eruption is quite the same as Meleney's type of ulcer I have seen several ulcers of the latter type, and they have been much more undermined than this One could insert a probe underneath the borders In this case the ulcers are sloping There is superficial

undermining of the upper epithelial layers, with a pink halo. The kidney shape and a piling-up of this erythematous portion are on the convex curve, while the concave area are flush with the skin. It certainly suggests a bacterial process of some sort. As far as dermatitis factitia is concerned, this may be a factor. The patient's wife says that when he is home he spends two or three hours a day changing his dressings. This would not account for the lesion on the posterior portion of the thigh, which is a place difficult for the patient to manipulate. As to the penicillin, he had over 2,000,000 units in the hospital. One large ulcer on his ankle healed quickly. Three or four small lesions refused to heal. As soon as he got home they all began to retrogress again. I think that the eruption is a mixed bacterial infection. I have had him in the hospital now for ten days with nothing but wet compresses of boric acid being applied. Some of the lesions have shown good progress, but the one on the thigh is perhaps a little larger. I am going to give him a full dose of sulfadiazine. I suppose that if this disease were seen in North Africa it would be regarded as desert sores.

#### **Necrobiosis Lipoidica Diabeticorum** Presented by DR HAL E FREEMAN

M D B, a white woman aged 35, has been a diabetic patient for eight years. The treatment for diabetes has included comparatively large doses of insulin. The lesions on the right leg and left foot have been present for five years.

There is an oval yellowish firm lesion on the dorsum of the left foot, about 2 cm in its longer diameter. It is on the site of an old scar produced by trauma fourteen years ago. On the right leg about half way between the knee and the ankle is a similar but larger hard discolored oval area about 4 by 8 cm. Surrounding this firm lesion is a quarter-sized ulcer having prominent margins. Its base is covered by indolent granulations.

There was much sugar in the urine. Determinations of the blood sugar level revealed between 290 to 350 mg per hundred cubic centimeters. The blood cholesterol level was between 334 to 173 mg per hundred cubic centimeters. The biopsy specimen from the edge of the ulcer showed areas of slight necrobiosis with a surrounding lymphocytic zone. No foam cells or xanthoma cells were present. Treatment has included treatment of the diabetes with insulin and diet, injection of insulin into the necrobiotic area, curettage and local application of Aloe vera leaf twice daily.

#### DISCUSSION

DR CLEMENT E COUNTER. These lesions are good examples of necrobiosis lipoidica diabeticorum. The patient's blood sugar level is high, even when she has no glycosuria. There is a factitial factor in the production of the ulcer. The patient has found hard concretions of cholesterol in the margins of the ulcer. She takes delight in picking them out and showing them to Dr Freeman.

DR NELSON PAUL ANDERSON. I think that one point which should be stressed is that one of the lesions of necrobiosis lipoidica diabeticorum has occurred in an old linear scar on the dorsum of the left foot. This scar resulted from an automobile accident in 1929. This is the first time that I have seen necrobiosis lipoidica diabeticorum occurring in an old scar.

DR HAL E FREEMAN. Dr Anderson's point is interesting. I knew about the automobile accident and the injury and had not paid any particular attention to the connection. I had not thought about the infrequency of necrobiosis occurring in scar tissue. It seems reasonable that such lesions might occur more easily in poorly nourished tissue than in normal tissue. Even though I fully realize that one is not expected to cure this disease, I believe that the patient is getting better.

#### **Monocytic Leukemia Cutis** Presented by DR HAL E FREEMAN

M E F, a white woman aged 59, was presented before this society five months ago. She has had pruritus for three and one-half years. There has been a gen-

eralized eruption for seven months. Four months ago there was extensive exfoliation. There have been various-sized cutaneous tumors, the largest of which were about 1 cm. in diameter.

There is a generalized erythematous squamous eruption. New subcutaneous tumors are on the lateral surface of the right hip and in the right axilla. Inguinal lymph nodes are larger now than when she was presented before this society four months ago.

The patient believes that she is gradually improving. She is more comfortable now than at any time since her eruption began.

Six determinations of the blood cells and hemoglobin in the past five months have shown a gradual decrease of hemoglobin from 12.5 to 9.6 Gm. The erythrocytes have fluctuated from as many as 4,500,000 three months ago to 3,500,000 five weeks ago. Leukocytes have gradually been reduced from 76,000 to 16,000. The differential studies on leukocytes showed about 10 per cent neutrophils and between 70 and 80 per cent lymphocytes and monocytes.

Treatment has included irradiation with low voltage roentgen rays, administration of solution of potassium arsenite by mouth and application of precipitated sulfur lotion locally.

#### DISCUSSION

DR PAUL FOSTER. I saw this patient when she was hospitalized in the White Memorial Hospital, seven months ago. The original blood count was high, but each day it kept going down. When she left the hospital the eruption had cleared entirely. This was over six months ago. This is the first time that I have seen her since. The eruption to me does not look anything like the original. When I first saw her she had purpuric areas, bullae and hematomas of the mouth. Tonight I should be unable to make a diagnosis from the clinical picture presented. I do not believe that the diagnosis is monocytic leukemia. I studied the slides, and at that time I saw very few monocytes. In my opinion they were lymphocytes, and if this is a leukemia it is a lymphatic leukemia and not a monocytic leukemia.

DR W. H. GOECKERMAN. I should think that objectively the only thing one could say is that she has an erythroderma. I wondered whether a competent hematologist had reviewed the blood picture.

DR FLETCHER HALL. The last blood count was made on Aug. 25, 1944, at which time the hemoglobin content was 9.6 Gm.

DR MOLLEURUS COUPERUS. When the patient was examined tonight, in the right axilla there were six or eight superficial nodules which may be local infiltrations of the skin. That perhaps would be a good site for removal of a biopsy specimen.

DR SAMUEL AYRES JR. What are the gradual improvement of the patient and the reduction of the white blood cell count based on? Are they based on the administration of solution of potassium arsenite or were other measures involved?

DR HAL E. FREEMAN. This case is presented with a great deal of humility. To begin with, if I am wrong in the diagnosis, I am happy for the sake of the patient. I believe that the lesions in the axilla are cutaneous and subcutaneous nodules and not enlarged lymph nodes. I do not know whether the improvement she has shown has been due to the solution or to the roentgen rays. If I had not felt satisfied with the diagnosis last spring, I would not have presented it so unequivocally. Arbitrarily, the peroxidase stains ruled out the diagnosis of lymphatic leukemia. She had no splenomegaly and no lymphadenopathy. To me, the cells were monocytes. The histologic section showed a cellular infiltrate which seemed to fit in with that diagnosis. A competent histopathologist in Rochester, Minn., has reviewed the histologic and the hematologic sections and can see no evidence in those sections of lymphoblastoma. He believes that the disease might be lichen planus. Of course, we know that it is not lichen planus clinically. Another competent pathologist in Philadelphia studied the same

sections, and a hematologist in the same institution studied them. They felt that these cells were lymphocytes and not monocytes. I do not know how they can be called lymphocytes though, in the presence of the positive peroxidase stain. The pathologist in Philadelphia believes that it might be a case of mycosis fungoides.

**Lupus Erythematosus** Presented by MAJOR I. M. HINNANT, M. C. (A. U. S.)  
(by invitation)

E. H. F., a young man, about 25, has had patches of alopecia for two years. There was some tenderness and sensitivity of the bald patches when they began. The last area began about five weeks ago. For a period of about two years he has had pain inside his mouth whenever he opened it widely. He was hospitalized at Mather Field for this complaint eleven months ago. Six months later there was a red scaly patch on the right cheek, just below the eye. This has gradually spread, and it has some sensation of itching and burning. His general health has been excellent.

There is a large atrophic scaly erythematous area of dermatitis on the right cheek which has dilated follicular orifices. On the scalp there are three plaques of alopecia characterized by mild erythema and considerable atrophy. Several areas of leukoplakia with erythema at the borders and some areas of atrophy are on the buccal surfaces of the cheeks.

General physical examination revealed no abnormalities. On roentgenologic examination the chest and the nasal sinuses were normal. Blood counts, results of urinalysis and sedimentation rate were normal. There were no dental foci of infection and no foci of infection in the nose or the throat. There was a normal temperature during the period of observation in the hospital. The prostate gland was normal. The serologic reaction for syphilis was negative.

Biopsy of the scalp revealed some thinning and atrophy of the epidermis. There was dilatation of the follicular orifices, with keratinous plugs. Infiltration with lymphocytes was present immediately around the appendages of the skin. The section from the mucous membrane showed acanthosis and dyskeratosis, with squamous cells remaining polygonal and vacuolated almost to the surface of the epidermis. Just beneath the epidermis was a dense infiltration of small round cells intermingled with large mononuclear cells.

#### DISCUSSION

DR ANKER JENSEN: This patient shows typical lesions of lupus erythematosus in three different kinds of skin all in the same person. Trying to make a diagnosis of the oral lesion without biopsy and the other lesions would have been difficult. I should have diagnosed lichen planus.

DR J. W. WILSON (by invitation): There must be some aspects of dissemination in order for the eruption to get to the mouth. I recall a patient with a lesion of the palate much like this man's mucous membrane lesions. My patient also had lesions on the palms and soles, none of which were exposed to the sun.

DR NELSON PAUL ANDERSON: I think that it is unusual to see a patient with lesions of lupus erythematosus on the scalp and face and in the mouth. There must be some systemic cause that produces lesions of this type. In the sections of the lesion on the scalp the histopathologic changes fit in with the deep infiltrated type of lupus erythematosus as described by Bechet. I agree with Dr. Jensen that the lesions in the mouth simulate lichen planus.

DR HAL E. FREEMAN: Is it not true that this man is entitled to and should be offered a certificate of disability for discharge from the army?

DR SAMUEL AYRES: The oral lesions are most interesting. While not at all common in lupus erythematosus, one does see them occasionally. It is a good thing to learn to differentiate the oral lesions of lupus erythematosus from those of lichen planus. In all the cases which I have seen, the oral lesions are



a beefy red with a whitish border, while in lichen planus there is more a reticulated whitish appearance throughout. I think that there is a distinct difference. Feeling that these eruptions are usually associated with foci of infection, I believe that this patient's sinuses bear investigation. He is said to have had chronic sinus infection.

DR. W. H. GOECKERMAN: Is it the general impression that the sun produces lupus erythematosus? There is no doubt that many patients with lupus erythematosus are photosensitive. Some of these patients when exposed accidentally to sunlight have a decided exacerbation. Sunlight is not the cause, they are simply photosensitive. To me, one of the interesting things is that penicillin does not do a bit of good in these cases. Most physicians who have had experience with it say that it is contraindicated. I now have a patient with the acute disseminated type. She has had 3,000,000 units without the slightest benefit.

DR. H. C. L. LINDSAY: In reviewing the literature on the causes of lupus erythematosus, two outstanding experts furnish evidence that a streptococcus is a causative agent of lupus erythematosus. These references are: Forman, L., *Disease of Skin Due to Streptococcal Infection, Some Observations on Intradermal Tests in Erythema Multiforme and Lupus Erythematosus*, *Guy's Hosp Rep* 81:110 (Jan) 1931, and Shaffer, L. W., *Role of Streptococcus in Etiology of Pemphigus, Lupus Erythematosus, and Erythema Group of Hematogenous Dermatoses*, *J Michigan M Soc* 36:292 (May) 1937.

MAJOR I. M. HINNANT, M. C., A. U. S. (by invitation): I do not know whether or not the patient Dr. Goeckerman was referring to was one seen at the Air Base. No one thought that penicillin would cure her. I saw this patient before she had penicillin. The only change that could be noted in her course was that the erythema was greatly reduced after the first day or two of the administration of penicillin. This was thought to be due to a decrease of toxin. It did not affect her prostration, malaise and anemia. She received large doses, and, as Dr. Goeckerman stated, she was unimproved. All patients of this type are discharged from the army as soon as it is considered that they have received maximum medical care. There is no hesitancy in removing them from the service. The present patient is from Chicago. He wants to be a farmer. He will be separated from the service as soon as he has received adequate medical care. He has had no treatment directed toward lupus erythematosus. Unfortunately, he has had much treatment directed topically for diseases which he does not have.

#### Chronic Allergic Dermatitis Presented by DR. H. C. L. LINDSAY

C. G., a young man aged 21, has had eczematous patches on the flexor surfaces of the elbows almost continuously since infancy. He was free from this eruption for one year just after coming to California from a state having colder winter weather. The eating of bread makes him worse. Contact with bakelite and wool irritates his skin. His skin is always worse during the winter. He had rickets when a child. One sister had eczema on her arms and attacks of severe asthma when she was a child. His mother had eczema in the axillary regions.

There is a dry scaling eruption distributed back of the ears and on the neck and the upper part of the chest. The scalp is free of scaling and redness. The eyelids are red and swollen as from chronic chafing. All areas involved are ill defined.

Previous therapy has included roentgen rays, autohemotherapy and intramuscular injections of an extract of spleen, all of which have given some benefit. Special eliminative diets have been of no benefit.

#### DISCUSSION

DR. JOHN ROGERS: The eruption could very easily be an atopic eczema. I believe also that there must be a seborrheic dermatitis connected with it. I think that combination is rather frequent, and sometimes it is difficult to be sure which is uppermost in the causation of the symptoms.

DR W H GOECKERMAN Has anybody ever seen a case of genuine atopic eczema cleared up through studies in allergy? I am frank to admit that I have not I still doubt that reported cures have been effected in cases of the true atopic type

MAJOR I M HINNANT, M C, A U S (by invitation) Dr Karl Figley, of Toledo, Ohio, did considerable work on sensitization to silk about fifteen years ago In his office, I have seen cases in which the patients had this type of eczema due to sensitivity to silk Unfortunately, there are not many cases of sensitivity to silk I have had the opportunity of finding 10 or 12 cases of sensitization to silk No other treatment, except that with soothing ointments, was able to bring about complete lasting cures when silk was eliminated I suggest that there is a large neurogenic factor in this person and that he would get more help from a psychiatrist than from an allergist Dr Figley proved that sensitivity to silk was a problem of sensitivity due to inhalation as well as to contact These patients have aggravation when in contact with silk, and Dr Figley proved that by inhalation of silk particles exacerbations would occur His work was carefully controlled, and his conclusions are reliable

DR PAUL FOSTER I think that sensitivity to silk lasts longer than any other When I was taking my postgraduate course in New York city, I allowed Dr Sulzberger to put a passive transfer test on my arm, and even to this date, over ten years later, on coming in contact with silk the two areas on my arm become swollen

DR SAMUEL AYRES I think it advisable to try the use of hapamine The manufacturers claim that sometimes in cases of life-long duration, three or four months may be required before one gets any results I have about 50 patients under treatment with hapamine, but I am not in a position to give any final opinion I have seen some interesting results, particularly in urticaria An extreme reaction to flea bites was stopped by its use

DR M E OBERMAYER Dr Ayres, do you give hapamine intracutaneously, and, if so, have you seen any reactions?

DR SAMUEL AYRES The recommendations are 0.01 cc intradermally and increase of the dose slowly by 0.01 to 0.05 cc up to 0.1 cc and then by 0.05 to 0.1 cc up to a maximum of 1.5 cc, these subsequent doses being given subcutaneously at intervals of four or five days I had a severe reaction in a patient in whom a reaction was least expected, that patient had pityriasis lichenoides chronica If the first intradermal injection causes much local reaction, it is an indication to increase the dose slowly or to start with a 1 to 10 dilution of the original concentration

DR PAUL FOSTER In regard to antigen H, or hapamine, I think that it is of definite value for atopic dermatitis, along with other measures I had one man in the hospital whom I started to treat with 0.1 cc doubling it until he was being given 10 cc at a dose Then I gave him 10 cc every four hours for about a week His skin cleared almost entirely, but on his leaving the hospital it flared up again It seems to me that if it is possible to give this substance in doses as large as this it cannot be very toxic

DR SAMUEL AYRES The recommended maximum dose is 1.5 cc

DR PAUL FOSTER This case of atopic dermatitis appears to me rather typical of the disease In the past two years I have had extremely good results in clearing the skin of this type of patient I found several years ago, by the use of the pH meter, that all patients with atopic dermatitis were on the alkaline side I first started giving them an acid ash diet, and later from 20 to 50 drops of diluted hydrochloric acid with each meal was added to therapy Finally their intake of beverage was restricted to distilled water, not only as a beverage but in the preparation of their food as well It was not until the latter portion of the treatment that I began to get the results desired One man who had been treated for ten or twelve years and who came to me from Dr Ayres is completely well and back

at work I feel that this method of therapy offers a good addition to the armamentarium for a disease which heretofore has responded to nothing

DR H C L LINDSAY These patients are all problem children Most of them are introspective Skin which sheds rapidly loses salt, and most such patients have salt imbalance Not infrequently they are benefited by the addition of salt to their diets One patient who was seen here seemed to get well by taking 1 teaspoon of table salt three times a day two hours after meals The patient presented today has been slightly benefited by injections of an extract of spleen Paul stated in the *Urologic and Cutaneous Review* for November 1921 "It (spleen extract) changes protrypsin from the pancreas to trypsin in the portal vein which is reached through the splenic vein, by the internal secretion of the pancreas Trypsin digests to albumins which have been absorbed from the intestines" I have tried injections of an extract of spleen on several patients both in the treatment of eczema and in the treatment of urticaria, and I have been agreeably surprised One patient with severe chronic allergic dermatitis recovered with intense doses of Panteric tablets and dilute hydrochloric acid in moderate doses, taken at meal time

#### Bird Scabies Presented by DR NELSON PAUL ANDERSON

L O, a white woman aged 42, has complained for the past two weeks of "hivelike" welts over most of her body Many of these resembled water blisters which had dried, leaving a hard center

The patient presents a generalized discrete erythematopapular eruption This is particularly evident on the trunk, arms, forearms and thighs There is involvement of the hands, the fingers and the insteps In occasional areas there are groups of erythematous wheal-like lesions with central puncta A superficial biopsy preparation was made from several of the papular lesions on the hands No *Sarcoptes scabiei* were found The patient was instructed to search her bedroom for minute living objects when it was learned that sparrows and pigeons nested in the gutters of her house Two permanent microscopic mounts of several organisms brought in by the patient are presented They are typical of so-called avian itch mite, *Dermanyssus avium et gallinae*, as illustrated in the article by Sulzberger several years ago (Sulzberger, M B, and Kaminstein, I Avian Itch Mites as Cause of Human Dermatoses, *ARCH DERMAT & SYPH* 33 60 [Jan] 1936)

According to a statement from her family (the patient was not informed), the patient has carcinoma of the cervix uteri In May 1944 she had a cesarean section followed by a hysterectomy

The patient has improved with starch baths and the local use of 2 per cent rotenone She was advised to get rid of the birds

#### DISCUSSION

DR PAUL FOSTER Avian scabies is probably more common than is generally supposed and probably the diagnosis is missed in many instances In the cases that I have seen the eruption has involved the upper portion of the back and shoulders and the back of the neck It has been a rather ill defined eruption with excoriations, and in none of the instances would it suggest scabies

DR M E OBERMAYER I feel fairly certain that the diagnosis is correct However, even some of us who have been especially interested in this field lack the entomologic knowledge which is required for the exact identification of such animal organisms The best procedure is to send such slides to an entomologist at the nearest university for verification

DR NELSON PAUL ANDERSON I thought that it was worth while to call attention to the fact that so-called bird scabies does occur Occasionally all dermatologists see patients with lesions resembling insect bites or suggestive of scabies and yet presenting no burrows and revealing no acari in epidermal

shavings examined under the microscope I am of the opinion that fleabites occur more frequently in September and October. Possibly there is a great increase in certain other types of insects at certain times of the year.

**Keratosis Follicularis in Mother and Daughter** Presented by DR NELSON  
PAUL ANDERSON

C S, a 36 year old housewife, is the mother of R S, a 14 year old school girl. The mother's father, who was one of eleven children, is said to have had the same disease as his daughter and granddaughter. The present eruption has existed in the daughter since shortly after birth and in the mother as long as she can remember.

Both patients present an almost generalized follicular papular keratotic eruption. Only the palms and soles are not involved. The papules are acuminate and give the skin a coarse, nutmeg-grater-like appearance and feeling. In some places an erythematous element is present. On other areas, such as on the sides of the neck, there is a dirty gray appearance. There is considerable scaling on the scalp of both patients.

Biopsy reveals pronounced follicular plugging, with hyperkeratotic masses filling the follicular orifices.

Treatment has included the use of 100,000 U S P units of vitamin A daily.

DISCUSSION

DR M E OBERMAYER One of the unusual features was the presence of follicular spines in some areas, thus the eruption is really a lichen spinulosus type of follicular ichthyosis. I am surprised at the response of the disease to the relatively low dose of 100,000 U S P units of vitamin A, for it has been my understanding that much higher doses are required.

**Periadenitis Mucosa Necrotica Recurrens** Presented by DR PAUL D  
FOSTER

K S, a white woman aged 29, was born in North Carolina. She has six brothers and sisters, a husband and two children, none of whom have a similar trouble. About twelve years ago the patient noted that the mucosa of her nose was swollen and that it was interfering with her breathing. About the same time her gums and eyes became swollen and red. Two years later white spots developed on her mouth, accompanied by swelling of her mouth and lips. The lesions got worse at her menstrual periods and practically disappeared during pregnancy. Eating nuts makes the disease worse. It is worse also in the summer. She has had excessive mucinous content of her saliva, and her teeth are always heavily coated. In the last few months there has been an increase of swelling and ulceration of the mouth and lips.

There are several sharply margined ulcerations with grayish white bases which are surrounded by narrow zones of inflammation. The grayish exudate cannot be wiped off. Lesions are on the mucosa of the lower lip, buccal mucosa and right pharyngeal tonsillar fossae. Small vitiliginous spots are present beneath her chin.

The tuberculin test elicited a normal reaction. The area of erythema resulting from an intradermal injection of smallpox vaccine was 10 cm in diameter. Results of various other tests, including cytologic studies of the blood, determination of blood sugar and urinalysis were all normal. The Wassermann reaction of the blood was negative.

DISCUSSION

DR H C L LINDSAY Lesions of periadenitis mucosa necrotica recurrens usually leave scars, especially when they involve the lips or genitalia. The center of an individual lesion turns necrotic and drops out, leaving a pit. It was thought at one time that the disease was due to tuberculosis. It may involve other members in a family. A child whom I presented some time ago had

lesions on the lip which were intensely painful. Scars from former lesions caused distortion of the lip. The grandfather of the child had had the same disease, and the mother had the malady at the same time of life that the child had it. Her lesions were also on the lips and the vulva. The disease tends to recur again and again.

DR SAMUEL AYRES: I did not see why that is not a case of ordinary herpes buccalis. The patient stated that the lesions were superficial and lasted only a few days. In periadenitis, in my opinion, the lesion is deeper, persistent and more painful.

DR M. E. OBERMAYER: I cannot agree with the diagnosis. This is a case not of periadenitis mucosa necrotica recurrens but of stomatitis aphthosa, the commonly encountered superficial type and not the comparatively uncommon deep form of the disease.

DR PAUL FOSTER: The lesions in this particular instance were not as indurated and fulminating as were originally described by Sutton and Loblowitz for periadenitis mucosa necrotica recurrens. But the history and course of the disease have been typical. There have been much severer occurrences in the past than at the present. As a matter of fact, since she has been given smallpox vaccine subcutaneously in doses up to 0.5 cc., the lesions are greatly improved, and if I had not seen the eruption until tonight, I would not think that it was periadenitis mucosa necrotica recurrens. Since the injections of smallpox vaccine, for several weeks she has had no lesions at all—the first time in many years. She is an extremely neurotic person. She is never happy, and nothing done for her is just right. She has never admitted that she is any better, but Dr. Eskelson and I noted an improvement after about the fifth injection of smallpox vaccine.

#### MANHATTAN DERMATOLOGIC SOCIETY

GEORGE M. LEWIS, M.D., *President*

WILBERT SACHS, M.D., *Secretary*

*Oct 10, 1944*

**Perivasculitis** Presented by DR. E. WILLIAM ABRAMOWITZ

Mrs. F. C., 32 years old and born in this country, complains of an eruption on the shins and ankles that has appeared during the summer and improved during the winter for the past twelve years. She came to my office on May 17, 1944, saying that the eruption had become more pronounced during the previous two weeks. She presented crusted and purpuric patches, from the size of a pea to that of a bean, around the ankles and extending up the shins.

She was seen at the New York Skin and Cancer Hospital in 1932 because of similar lesions. A biopsy was reported as indicating the presence of perivasculitis. The hemogram and the bleeding and coagulation times, determined on July 12, 1944, were normal. The vitamin C content was reported as slightly low at that time. The urine showed a faint trace of albumin.

The patient was given two injections of hapamine, an azohistamine preparation, for the purpose of desensitization, without effect. She was then given daily doses of 250 mg. of ascorbic acid. New lesions have continued to appear, but they are not as painful as formerly.

She is presented for suggestions as to therapy.

#### DISCUSSION

DR. ANTHONY C. CIPOLLARO: I agree with the diagnosis as presented, chiefly because I do not know into what other category to put the disease.

DR FRED WISE I agree with Dr Cipollaro, and I believe that the patient would derive great benefit from the application of a gelatin-zinc oxide bandage

DR MAURICE J COSTELLO I agree with Drs Cipollaro and Wise, but I believe that the patient should receive gold sodium thiosulfate intravenously. In the case of a patient presenting a similar condition, who was shown before this society, the eruption cleared completely with this form of therapy

DR HERMAN SHARLIT I am interested in the therapy suggested by Dr Costello. Will he tell us more about it?

DR E WILLIAM ABRAMOWITZ I am thankful for the therapeutic suggestions. I looked at the slide of the biopsy specimen taken at the New York Skin and Cancer Hospital in 1932, and there was pronounced destruction of the vessels in the cutis, with no sign of tuberculosis or tuberculid. I thought that the patient had some cryptic infection and that the eruption on her legs was an allergic manifestation. She had a rather low vitamin C level, and I therefore gave her large doses of ascorbic acid by mouth. There was a slight effect but not enough to justify continuation of the treatment. I should like to hear from Dr Costello on what basis gold would be indicated for a purely destructive vascular lesion, as gold has an unfavorable effect on the vascular system

DR MAURICE J COSTELLO In answer to Dr Sharlit's question, the patient of whom I spoke was presented before this society on several occasions. She gave a family history of tuberculosis. I thought that the eruption was of tuberculous causation, hence I treated her with gold sodium thiosulfate, a drug which has at times been successful in the treatment of dermatoses of tuberculous origin.

#### **A Case for Diagnosis (Bazin's Disease, Multiple Thromboses?) Presented by DR ANTHONY C CIPOLLARO**

D C, a woman aged 50, consulted me on May 26, 1944, stating that she had had trouble with her legs for about twenty-five years. She complained that varicose veins and lumps would appear and disappear on various portions of her legs for all these years. Last year she had phlebitis, and a few months later she underwent an operation for varicose veins, which consisted of ligation of the internal saphenous vein bilaterally. After the ligation she had about fifteen injections into different varicosities. Recently she had been complaining of burning pain in both legs and the development of hard nodular lesions which do not ulcerate. A biopsy of one of the hard nodular lesions was reported as showing that it was "lipofibronema."

An internist made a complete physical examination including serologic tests of the blood and determinations of basal metabolic rate, with negative results. The only significant abnormalities were those referable to the legs, including "moderate arterial insufficiency in the left leg and a few residual varicose veins which I do not think have any connection with the nodules."

The patient now presents several hard nodular subcutaneous lesions varying in size from that of a pea to that of a peach, scattered over both legs, being most prominent on the dorsal surfaces. The overlying skin is red, and the lesions are firm. There are no ulcerations and no scars from previous ulcerated lesions.

The patient has been treated with intravenous injections of gold sodium thiosulfate, with some improvement.

#### **DISCUSSION**

DR FRED WISE The clinical picture is that of Bazin's disease. The only objection to that diagnosis clinically is the fact that lesions are present on the arm, but in an exceptional instance the same pathologic changes might occur on the upper extremities to a less advanced degree than on the lower, and the fact that there are lesions on the arm would not deter me from making a diagnosis of Bazin's disease.

DR MAURICE J COSTELLO I agree with Dr Wise I have seen patients with Bazin's disease on the upper extremities

DR MAX SCHEER I thought that some of the lesions which this patient presents were venous thromboses

DR HERMAN SHARLIT I agree

DR PAUL E BECHET I should agree with a diagnosis of erythema induratum

DR MIHRAN B PAROUNAGIAN I also agree with Dr Wise's remarks

DR GIRSCH D ASTRACHAN The fact that the patient presents lesions on other parts of the body besides the legs does not rule out Bazin's disease A few years ago at the New York Academy of Medicine I presented a patient with Bazin's disease who had lesions on the upper and lower extremities (ARCH DERMAT & SYPH **34** 316 [Aug] 1936) Because of the extreme tenderness of this patient's lesions, however, one may have to consider the possibility of a persistent erythema nodosum of some toxic origin combined with Bazin's disease

DR E WILLIAM ABRAMOWITZ Certainly the lesion on the calf is typical of Bazin's disease, although the patient's age, the lesions on the rest of the body and the duration are not in favor of that diagnosis The biopsy does not show it I think that several other possibilities must be taken into consideration here, one of which is the ingestion of iodides or bromides Another is nodular nonsuppurative panniculitis If these can be excluded, I shall be willing to accept a diagnosis of Bazin's disease

DR FRED WISE If a lesion shows a distinct depression, as in this case, is that not an indication of a previous breaking down of tissue?

DR ISADORE ROSEN The clinical manifestations did not give me the impression that they were related to Bazin's disease The lesions are raised and inflammatory and show no evidence of ulceration I suggest studies of the lipids in the blood in this case to rule out some allied process

DR ANTHONY C CIPOLLARO I considered this to be a case of Bazin's disease, but because of the lack of ulceration I tended more toward a diagnosis of damage to the vascular system I am glad that Dr Abramowitz and Dr Rosen brought out the possibility of some lipid dystrophy, and I am going to study the patient from that standpoint I treated her with injections of gold sodium thiosulfate After four injections the lesions had practically disappeared, and she then went away for a vacation When she returned, the nodules were much larger than they were before treatment, that made me think that it was a breakdown of tissue around the vessels, and I then considered the lesions to be thromboses rather than a tuberculous process

#### Ocular and Oral Pemphigus Presented by DR MAURICE J COSTELLO

M B, a German-American married woman aged 56, was first seen about six months ago in the ophthalmologic service at Lenox Hill Hospital At that time she was admitted for canthotomy because of symblepharon of the right eye following pemphigus, which had been confined to this organ for several months Later bullous lesions developed on the palate and mucous membranes, and they are present this evening

Treatment has consisted of twenty injections of phenarsone sulfoxylate, 1 Gm. intravenously at weekly intervals

When the patient was first observed, she had no constitutional symptoms, but she has lost weight and strength during the past six weeks and has had frequent gastrointestinal disturbances accompanied with severe pain in the abdomen and chest

In spite of the fact that she appears to be anemic, the hemoglobin content is 105 per cent The blood count showed erythrocytes, 5 000,000, and leukocytes, 7 100, with 56 per cent polymorphonuclear leukocytes (12 per cent immature), 36 per cent large lymphocytes and 8 per cent eosinophils

## DISCUSSION

DR MAX SCHEER I agree with the diagnosis

DR HERMAN SHARLIT I am curious to know why the adhesion of the lids to the eyeball was not prevented. If some material were interposed between the lids and the eyeball, the adhesions could not form.

DR ANTHONY C CIPOLLARO I should like to hear a discussion on the management of such cases.

DR MAURICE J COSTELLO This patient when first seen had bullous lesions of the uvula and the palpebral conjunctivas. She was treated with phenarsone sulfate because of the good results which have been obtained with acetarsone at Bellevue Hospital in patients with pemphigus vulgaris. The ophthalmologists have performed canthotomies on several occasions.

### Spiegler-Fendt Sarcoid Presented by DR ANTHONY C CIPOLLARO

H M., a woman aged 42, was previously presented at the New York Academy of Medicine, on April 7, 1936. She first attended the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in May 1935, at which time she had several brownish elevated lesions, varying from the size of a pinhead to that of a small pea, scattered over various portions of the face. There was a scar on the left cheek, resulting from surgical removal of one of these large lesions. Repeated biopsies have been performed, and all confirm the diagnosis of Spiegler-Fendt sarcoid. The lesions were treated with roentgen rays. To each lesion, closely shielded, was administered a dose of  $\frac{1}{2}$  erythema dose (275 r) of medium voltage (135 kilovolts) filtered (3 mm of aluminum) rays. Some lesions cleared as the result of a single treatment. Others required a repetition of this treatment after an interval of three weeks. The patient returned to the clinic once or twice each year since 1935 because lesions developed, and these responded promptly to irradiation in the aforementioned doses. Lately the lesions have been treated with low voltage (100 kilovolts) unfiltered roentgen rays in doses of 225 r. The latest lesion which has developed appeared about two months ago on the right side of the nose. This is one of the largest lesions that the patient has ever presented. It is the size of a large pea and of a brownish red color. The consistency is firm but not hard.

The patient has had repeated examinations. The Wassermann reaction of the blood was negative, and the results of urinalysis and blood counts have been repeatedly normal. The basal metabolic rate was +12 per cent. Roentgen ray examination of the long bones revealed no abnormalities. A roentgenogram of the lungs showed moderate hilus and root branch thickening—old Ghon nodes. Roentgenologic examination of the gallbladder showed a functionally competent organ. Ophthalmologic examination revealed normal conditions. The general physical examination, including a pulmonary examination, revealed no abnormalities. Gynecologic examination showed pronounced cervical erosion, endocervicitis, nabothian folliculitis and vaginitis due to *Trichomonas vaginalis*. She had a cauterization of the cervical canal and was treated for the vaginitis.

## DISCUSSION

DR WILBERT SACHS It is difficult on hasty examination of the lesions to say that this is a case of Spiegler-Fendt sarcoid. One would have to know the history and the type of lesion that was present before. In view of the fact that biopsy was performed on previous lesions and the same diagnoses made several times, there is a strong presumption that this is the same type of lesion. There is no clinical way of making an absolute diagnosis of Spiegler-Fendt sarcoid for a single lesion, but I should of course agree with that diagnosis in view of the history.

DR GEORGE M LEWIS I wonder whether epithelioma was considered as a possibility. On clinical grounds alone, the pale color and the telangiectasia over



the surface would make me suspect it, irrespective of the past history. The lesions of Spiegler-Fendt sarcoid are usually reddened papules or nodules.

DR FRID WISE. All dermatologists know that Spiegler-Fendt sarcoid is one of the rarest of cutaneous diseases, and I should be unable to venture a diagnosis for the lesion of the nose. In fact, I should hesitate to make a diagnosis of Spiegler-Fendt sarcoid for any part of the body without histologic investigation. In view of the lesions on other parts of the body, I should say that this is probably another lesion of the same disease, but histologic confirmation is necessary.

DR MAURICE J. COSTELLO. When I was associated with Dr. Howard Fox, I saw a patient with lesions on the lower part of the back, which he stated had been present for thirteen years and had not increased in size during that period. Biopsy revealed Spiegler-Fendt sarcoid. The lesions were treated with roentgen rays and disappeared after two or three treatments. Satellite lesions then developed which were even more sensitive to roentgen rays than the original lesions were. I believe that Spiegler-Fendt sarcoid is more sensitive to roentgen therapy than ordinary sarcoid is.

DR ANTHONY C. CIPOLLARO. It is difficult to make a diagnosis of Spiegler-Fendt sarcoid without biopsy, but I have been watching this patient since 1935, and she has repeatedly shown lesions similar to the one she presents tonight, although most have been smaller. The lesions are firm but not hard, have a brownish red color, have no infiltrative border and do not ulcerate. All the lesions treated have responded to either one or two exposures to filtered or unfiltered roentgen rays, showing that these lesions are radiosensitive to either form. The lesion now present so closely resembles all other lesions that I did not feel justified in performing a biopsy.

**A Case for Diagnosis (Streptotrichosis, Dermatitis Factitia?)** Presented by DR THOMAS N. GRAHAM

R. B., a white woman aged 35, was first seen by me on Aug. 15, 1944. She complained of an eruption of five years' duration involving the face and stated that she had had a series of "abscesses and boils" which began after the removal of infected tonsils. According to the history given by the patient, the lesions first appeared as painful lumps under the skin which subsequently broke through, producing a purulent exudate. The patient stated that the lesions were so painful that at times she had expressed their contents by inserting a sterilized needle or by using tweezers, after which they healed spontaneously. An exuding lesion on the right cheek has been present for one year. The patient has lost 30 pounds (13.6 Kg.) in weight since the onset of the disease.

The patient has been treated previously at the Hospital for the Ruptured and Crippled, the New York Skin and Cancer Hospital, Memorial Hospital and Vanderbilt Clinic. She was given general physical examinations, including examination of her sinuses, all of which revealed no pathologic changes. At two of these institutions she was apparently considered to have a dermatitis factitia. Serologic tests of the blood, cultures of blood, studies of blood chemistry, cultures of the lesions, studies of basal metabolism and a biopsy were performed, and roentgenograms were made. The patient was told that none of these tests revealed any pathologic changes. She was treated with numerous lotions and ointments, including sulfonamide ointments, and with roentgen ray therapy.

There are a number of scars on the forehead, cheeks and chin, the sites of previous lesions. On the right cheek, 3 cm. from the ear, there is a discharging sinus from which exudes a seropurulent exudate. There is retraction of the skin and underlying tissue around the sinus, which produces a depression in the right cheek. On the left cheek is a similar but smaller sinus. A number of subcutaneous nodules can be palpated in the areas around these sinuses.

A mycologic report, from the New York Hospital, by Miss Mary Hooper states "Microscopic examination showed dense masses with much fibrous material (no

granules with ray cells) Culture showed blood agar—*Staphylococcus aureus*, sodium thioglycollate—anaerobic granular colony—short rods, gram positive + —, nonmotile, non-acid-fast Colony masses in lactophenol pseudobranched Anaerobic *Actinomyces bovis*”

## DISCUSSION

DR ISADORE ROSEN I am more inclined to the diagnosis of dermatitis factitia. The irregularity of the lesions and their excavated character impress one that they are of artificial origin. Lesions of streptotrichosis are smaller and of more uniform character.

DR ANTHONY C. CIPOLLARO I saw this patient on several occasions, and my impression was that she had a factitious dermatitis, and this is still my impression. I am not disregarding the laboratory data. If repeated studies show streptotrichosis, that diagnosis will have to be accepted.

DR FRED WISE Both diagnoses should receive consideration before one arrives at a final decision. The patient said that there were nodules under the unbroken skin, and if this is so dermatitis factitia can be eliminated. Nodules with an unbroken epidermis point to a lesion which is not self-inflicted.

DR MAURICE J. COSTELLO For the reasons given I think that the patient has dermatitis factitia.

DR MIHRAN B. PAROUNAGIAN That is my impression also.

DR HERMAN SHARLIT It is difficult to determine such a diagnosis for a person who is hysterical. She may induce some changes herself, or the reaction may be secondary to some other disturbance. The only way to decide is to make further studies. The patient may be falsely accused of initiating a process which she merely aggravates.

DR JACK WOLF I agree with the diagnosis of dermatitis factitia. I cannot recall a single patient who attacked a dermatosis with instruments—usually forceps—who had anything but dermatitis factitia. I do not refer of course to the common acne “picker.”

DR DAVID BLOOM Because of the bacteriologic report, further study is necessary in order to confirm or definitely to refute the diagnosis of streptotrichosis.

DR PAUL E. BECHET In my opinion, both of these diagnoses are correct. Because the diagnosis of this rare disease depends entirely on laboratory identification of the fungus, the statement of Dr. Graham that it was found in this case is conclusive proof of the diagnosis. One knows that the disease presents gummatous or furunculoid infiltrations, and their appearance in a neurotic person might well induce the self-mutilations observed in Dr. Graham's patient. The clinical picture is definitely that of an artefact.

DR WILBERT SACHS When tissue is taken from a lesion which has been present for a long time, the histologic examination is naturally inconclusive. The patient is supposed to have deep nodules, and I suggest that one be removed. It would not add greatly to the scars already present. Something may then be found pathologically.

DR E. WILLIAM ABRAMOWITZ I am surprised that in all these years some attempt has not been made to rule out an artificial eruption. The chances are that it is factitious more than anything else. I do not see why the face cannot be covered by an occlusive dressing and kept so for a few weeks. In case that there is no change, the patient might be given potassium iodide and the results observed.

DR GEORGE M. LEWIS We all seem agreed that there is a factitious element, hence the question is whether the finding of *Actinomyces* and the presence of deep nodules can be ignored and the whole eruption considered dermatitis factitia. Certainly anaerobic actinomycetes are not common contaminants. I am of the opinion that this eruption should not be called dermatitis factitia until further study settles

the mycologic phase once and for all. A second deep biopsy as suggested might be productive of information, even with a negative result.

DR THOMAS N GRAHAM. I agree with Drs Wise, Sharlit and Lewis that the case should not pass off as one of dermatitis factitia. Definite subcutaneous nodules have been seen before they form sinuses, and these sinuses have healed rapidly after the contents of the nodules have been expressed.

**Dermatomyositis with Raynaud's Phenomena** Presented by DR MAURICE J COSTELLO

J F, a married woman aged 42, presents a generalized progressive scleroderma and dermatomyositis associated with acrosclerosis and Raynaud's phenomena. A thyroidectomy was performed in 1940 without relief of symptoms. The patient has had pain in her fingers for twenty years, and there is severe blanching of the fingers. At present, the scleroderma affects the hands and forearms in gauntlet-like fashion. There are contraction, thinning and tapering of the fingers, with many scars representing healed ulcerations, and the patient is unable to extend the fingers of either hand. Her immediate complaint is an intertriginous oozing fissured eczema of the inframammary regions, the inguinal areas and the intergluteal cleft. She also has a number of flat erythematous lesions from the size of a pea to that of a coffee bean, surmounted by flaccid vesicopustules. The patient is presented this evening so that the members may make mental note of her appearance prior to the administration of dihydrotachysterol.

DISCUSSION

DR E WILLIAM ABRAMOWITZ. I agree with the diagnosis of Raynaud's disease. I never was converted to the acrosclerosis terminology. As to the dermatomyositis, more conclusive proof should be submitted through biopsy of muscle tissue. Dr Costello says that he is showing the patient because he is going to give dihydrotachysterol and expects to present her again with good results. I hope so. A patient of mine with generalized scleroderma, sclerodactylia and Raynaud's syndrome of the hands and feet, who was receiving large doses of dihydrotachysterol for four or five months and, in addition, neostigmine bromide, died in spite of the treatment. There was involvement of the esophagus and aorta causing a disturbance of the cardiac rhythm and other symptoms. I have more confidence in baking and massage than in any internal medication for scleroderma. I think that little progress has been made in the treatment of this disease after it becomes generalized.

DR. FRED WISE. I agree that it would be desirable to get further evidence of dermatomyositis, and I would ask Dr Costello to report at the next meeting whether he has found further evidence of that disease.

DR HERMAN SHARLIT. In these cases the sclerodactylic feature is not altogether hopeless. I myself have seen cases in which the patients have improved, and Dr Lewis presented a patient who said that she was much improved after an operation for stripping the arteries. I think that the prognosis is quite hopeless from the point of view of internal remedies.

DR GIRSCH D ASTRACHAN. All cases of dermatomyositis which have been described in the literature have had three cardinal signs: (1) edema, (2) cutaneous eruption, which may be urticarial or erythematous, and (3) myositis. The last can be proved by biopsy. The fact that the patient complains of pains does not necessarily confirm the diagnosis of myositis. Pains do occur in cases of plain scleroderma. If this is a case of dermatomyositis, I should like to draw attention to Dr Sulzberger's case of dermatomyositis in which the patient was treated with injections of alpha tocopherol (vitamin E) intramuscularly and vitamins A and D orally and reported as much improved (*ARCH DERMAT & SYPH* 44 719 [Oct] 1941).

DR GEORGE M LEWIS In a series of cases of dermatomyositis seen at New York Hospital during the past few years, the symptoms have ranged all the way from the classic ones described by Dr Astrachan to ones approaching those in the case presented tonight. Dr Costello has followed this case, and if he has found muscular weakness of severe degree I think that dermatomyositis must be considered on that basis alone. Some of these patients get well spontaneously, hence the fact that the patient is better now is not against that diagnosis. What is seen tonight would fit in better with a diagnosis of scleroderma, but the previous observations of Dr Costello cannot be neglected.

DR MAURICE J COSTELLO Generalized scleroderma is frequently associated with dermatomyositis. One of the most reliable symptoms that I know of is the early inability of the patient to stand in bare feet without pain—a symptom which this patient presents. I put her on a wide table and asked her to turn from the prone to the supine position, it took her at least a minute to do so, because she lacked the muscular power to do it faster. One must remember that this patient's disease has been going on for ten or twelve years and that it has improved spontaneously. She gives a history of muscular weakness, inability to carry packages, and pain whenever the muscles are pressed during massage.

**Idiopathic Multiple Hemorrhagic Sarcoma (Kaposi)** Presented by Dr  
GIRSCH D ASTRACHAN

C J, an Italian man aged 79, registered on June 2, 1944 at the Metropolitan Hospital Dispensary, giving a history of an eruption of about fifteen years' duration on both feet and the left hand. An eruption appeared on the right hand about two and one-half years ago.

The right hand, including all fingers, is noticeably edematous and light bluish. Deep pitting can be produced on pressure. Over the surface are scattered many elevated indurated dark gray to brownish nodular lesions, varying in size from that of a pea to that of a bean. Some nodules have a smooth, shiny surface, and others are verrucous, with scanty adhering scales. A few lesions are somewhat ulcerated and covered with a thick, dark brownish crust.

On the back of the left hand and involving the lower part of the forearm there is a well defined, slightly elevated, irregularly shaped area of purplish infiltration. The border of this area is slightly elevated and nodular. A few nodular lesions are present on the palmar aspect of the left hand.

Both feet present diffuse well defined elevated indurated purplish-grayish plaques with a raised border. Over the lower parts of both legs are scattered a few nodular lesions.

Ten roentgen irradiations (75 r each) have been given to the right hand.

Laboratory data were as follows. The Wassermann and Kahn reactions were negative. The urine was normal except for an occasional hyaline cast and a very faint trace of albumin. The blood count was normal except for a red cell count of 4,210,000 and slight anisocytosis.

Determination of blood chemistry revealed an icterus index of 8 units and a sugar content of 93 mg, a urea nitrogen content of 13.8 mg, a uric acid content of 4.2 mg and a cholesterol content of 182 mg per hundred cubic centimeters.

Histologic examination of tissue removed from the back of the hand confirmed the diagnosis of Kaposi's sarcoma. The description by Dr Taub stated that the specimen consisted of whorls of hyperplastic connective tissue bundles showing pronounced vascularity, within these whorls were many areas of collagenous and fibrinoid degeneration with definite hemorrhagic extravasations. The connective tissue showed no sarcomatous change. Many endothelial cells were also present, but these did not appear malignant. The picture was felt to be one of the end stage of Kaposi's sarcoma.

The same tissue was examined by Dr Wilbert Sachs, who reported that at one edge of the section there was a tremendous mass composed of blood vessels,

connective tissue and cellular elements. The overlying epidermis showed no important change. In the upper portion of the mass were numerous dilated blood and lymph vessels and a tremendous amount of hemorrhage. There was some increase in connective tissue and a diffuse spindle cell infiltration. There was little or no connective tissue in the lower portion of the mass, and the spindle cells were densely packed. His diagnosis was "Kaposi's sarcoma with spindle cell sarcoma developing from it."

## DISCUSSION

DR MAX SCHEER. The lesions on the foot are those of Kaposi's sarcoma, but those on the hand looked different. They suggested prickle cell epithelioma.

DR HERMAN SHARIT. The lesions on the right hand give me the impression that increased malignancy is developing. It is possibly frank sarcoma.

DR JACK WOLF. This man presents the typical end result of long-standing Kaposi's sarcoma. All the elevated verrucous lesions, if not already sarcomatous, will soon show the histologic picture of spindle cell sarcoma. In view of the patient's age, I should be inclined to adopt a conservative attitude and destroy the lesions by means of electrodesiccation. The prognosis in such far advanced cases is invariably bad.

DR E. WILLIAM ABRAMOWITZ. One can speculate about the lesions on the hand, but those on the feet are classic examples of Kaposi's sarcoma. My idea would be that the patient has probably had the disease for some years and that somebody gave him arsenic. Some of the hyperkeratotic verrucous lesions gave me that impression.

DR ISADORE ROSEN. I agree with the remarks made by some of the previous speakers regarding the unusual features of this case. There are instances in which lesions of Kaposi's sarcoma undergo rapid proliferative changes with metastases, and the lesions on this man's hand strongly suggest such a process. It is not unusual to see vegetating lesions associated with Kaposi's sarcoma, especially on the feet, but these hypertrophic ulcerative tumors are rare.

DR ANTHONY C. CIPOLLARO. I think that Dr. Wolf covered the clinical ground in saying that this is a case of Kaposi's sarcoma with sarcomatous changes. I think that the verrucous lesions are typical of spindle cell sarcoma, and, with that in view, I would treat each lesion individually with filtered roentgen rays, 300 r every other day, until a total dose of 4,000 r has been given to each lesion.

DR FRED WISE. I am in agreement with the speakers who consider all lesions in this patient as Kaposi's sarcoma, whether they show spindle cell sarcoma microscopically or not. The verrucous lesions are rather common, especially adjacent to the big toes. In my experience at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, 3 patients have been treated with unfiltered roentgen rays without benefit and then with filtered radiation with favorable response.

DR GIRSCH D. ASTRACHAN. There are certain interesting features in this case—first, the age of the patient—80 years—and then the advanced stage of the eruption on the right hand. There are several prominent verrucous lesions with ulcerations, which are not often seen. A case of Kaposi's sarcoma with ulcerations was presented by Dr. Wise (*ARCH. DERMAT. & SYPH.* 47:733 [May] 1943). According to Dr. Sachs, the histologic examination shows changes characteristic of spindle cell sarcoma. This is an important complication, and I am much concerned about the treatment of this patient. I think that electrosurgical removal would not be advisable in this case. Removal of so many lesions for a man of 80 is a serious procedure. I should be inclined to follow Dr. Cipollaro's advice about high voltage roentgen ray therapy.

**A Case for Diagnosis (Xeroderma Pigmentosum?)** Presented by DR THOMAS N GRAHAM

A G, a white boy aged 16, was first seen at the New York Hospital on April 21, 1944, complaining of an eruption of three years' duration involving his face. There were no subjective symptoms. The patient stated that the eruption had become aggravated by exposure to sunlight during the preceding two summers. There was no family history of a similar eruption.

The skin of the nose shows erythema, keratotic papules, a few vascular papules and numerous deep-pitted scars. There are a similar but less pronounced eruption on the adjacent areas of the face and a few scattered lesions of the same type on the remainder of the face. There are a few discrete vascular papules. There are numerous pigmented macular lesions involving the entire face and the exposed areas of the neck, chest and upper extremities. The skin of the face is excessively dry. Within the past month an indurated erythematous lesion 1 cm in diameter has appeared on the right side of the nose. There have been no other lesions suggesting malignant degeneration.

The Mazzini test of the blood elicited a negative reaction.

Examination of the urine for hematoporphyrin (test of Watson and Schwarts) showed a trace of porphyrins to be present.

Conditions observed at biopsy, reported by Dr N Chandler Foot, proved to be consistent with a diagnosis of xeroderma pigmentosum. There were early proliferative changes without much metaplasia of the cells but with a considerable disarrangement of the normal architecture of the epidermis, and he concluded that the biopsy specimen was from a hypertrophic area in a xerodermatous lesion.

#### DISCUSSION

DR MAX SCHEER: I agree with the diagnosis. The patient has the dark freckles of xeroderma pigmentosum over his face, but the lesions on the nose look more like those of adenoma sebaceum.

DR HERMAN SHARLIT: I accept the diagnosis, and I think that the remarks made by Dr Scheer are in order.

DR ANTHONY C CIPOLLARO: I agree with the diagnosis.

DR FRED WISE: I also agree.

DR THOMAS N GRAHAM: There have been some lesions resembling those of adenoma sebaceum, but these lesions have disappeared spontaneously, and I believe that those of adenoma sebaceum do not.

**Subacute Disseminated Lupus Erythematosus** Presented by DR JACK WOLF

S N, a man aged 25, was referred to me on Oct 6, 1944 for treatment of an eruption of approximately three years' duration. The eruption had appeared with dramatic suddenness after a sunburn at the beach. Except for the past few months the patient has been continuously under treatment. Treatment has consisted of numerous injections (more than fifty) of a gold salt, many injections of bismuth subsalicylate, some concurrently with the gold, and injections of crude liver extract and the Hollander treatment with quinine administered internally and iodine applied to the lesions locally. The response to all treatment has been poor.

The patient presents a severe and diffuse process. There are irregularly oval atrophic telangiectatic spots with surrounding pigmentation on the face and neck, giving a dirty brown appearance to the entire area, there are numerous interlacing red strands approximately  $\frac{1}{2}$  inch (1.3 cm) in width, the central portion of which is atrophic, and the erythematous areas are mildly edematous and telangiectatic, diffusely spread over the anterior and posterior aspects of the chest, the arms and, to a lesser degree, the forearms. The patient presents diffuse alopecia and atrophic and telangiectatic spots on the scalp, the eyebrows are considerably thinned. The buccal mucosa, the palate and tongue are also affected.

and present acutely erythematous smooth and edematous spots, the vermillion border of the lips is telangiectatic, with numerous small atrophic strands

In spite of the severity of the process, the patient appears in fairly good health and is able to carry on a normal existence

## DISCUSSION

DR HERMAN SHARLIT I get the impression that there has been so much therapy that the patient should be given a rest for a while

DR E WILLIAM ABRAWOWITZ I think that the patient should be treated All dermatologists encounter eruptions that are resistant to all kinds of treatment One suggestion would be that he receive some preparation of gold other than the one already administered There are several on the market I understand that the sulfonamide compounds have not been tried, and once in a while results are obtained from them when used internally At the last meeting of the American Dermatological Association, Dr Cannon presented cases in which the patients were treated with strong solution of iodine U S P, that might be tried in this case An occasional transfusion of blood may be of help

DR ISADORF ROSEN In view of the extensive involvement, I urge that the patient be hospitalized and investigated from every angle as to the cause I suggest use of a different preparation of the same drug plus the administration of liver extract and a high vitamin diet In other words, it is important to build up the general health of the patient, in addition to other therapy

DR FRED WISE The patient should receive treatment if only for the reason that if he does not he will go to another physician or another clinic Another point to consider is the question of how much gold he received and what dosage was given

DR THOMAS N GRAHAM Benefit has been obtained in some cases of this type with vaccine therapy

DR MAURICE J COSTELLO At one time I had at Bellevue Hospital 4 cases similar to this one, and I hospitalized the patients and administered Germanin (sodium salt of the symmetric urea of metaamidobenzoylmetaaminoparamethylbenzol-levonaphthylamino-4,6,8-trisulfonic acid) One patient, whom Dr Bloom will recall, had had the eruption for eight years, and it completely cleared Other patients improved, but the drug had to be discontinued because of toxic reactions I have used the Winthrop preparation Naphuride, but I did not get the same results One other suggestion would be the administration of graded tuberculin in extremely small doses

DR MAX SCHIFFR It seems that every type of therapy has been recommended here except penicillin

DR JACK WOLF In addition to the various measures suggested, I have also considered the advisability of treating the patient with the ethyl chaulmoograte Good results with this agent have been reported in long-standing, resistant cases

DR GIRSCH D ASTRACHAN I noticed that no one mentioned giving bismarsen, as recommended by Weiss, Conrad and Pfaff (ARCH DERMAT & SYPH 44 1009 [Dec] 1941) I agree, however, with Drs Sharlit, Parounagian and Rosen that this patient should be treated cautiously, because he has received so many forms of therapy If bismarsen or bismuth is given, it should be in small doses and each injection should be accompanied with an injection of crude liver extract

DR JACK WOLF This man had three injections of oxophenarsine hydrochloride, and an exacerbation followed each injection I should be inclined to avoid any arsenical preparation Extreme caution in employing any active agent is required in this type of case

**Persistent Edema of Hands and Forearms** Presented by DR DAVID BLOOM

A C, an Italian janitor aged 48, came to the Skin and Cancer Clinic in September 1944, complaining of a recurrent eruption on the hands and feet of three years' duration

The palms and soles present an erythematovesicular eruption. The backs of both hands and the distal half of both forearms are decidedly edematous, but the skin covering this area does not show any signs of inflammation. Pressure does not leave any pitting in the edematous region.

The patient states that the edema of the hands and forearms has been present for two years. One year ago he suffered an attack of swelling and redness of the hands which cleared within one week following application of wet dressings. According to the patient, the swelling varies in size at different times.

No other member of the family, including his four grown-up children, has a similar condition. The past history of the patient did not reveal any illness except the eczematous eruption on the hands and feet.

## DISCUSSION

DR E WILLIAM ABRAMOWITZ. I presented a patient with an eruption of this kind and also 1 with severe elephantiasis of the scrotum of many years' duration with recurrent attacks of redness and lymphangitis. For the latter, the only measure that kept these attacks from reappearing was the long-continued use of sulfonamide compounds. Finally, his family physician gave him penicillin, and he has not had an attack in the four months since.

DR FRED WISE. The history in this case is indicative of a streptococcal or staphylococcal infection. Treatment with vaccines or penicillin should be tried.

DR JACK WOLF. I do not believe that the dermatophytosis of the feet bears any relation to the edema of the hands. Several patients with similar edema of the hands of unknown origin have been presented before this society within the past two years.

DR MAURICE J COSTELLO. I suggest a sulfonamide compound or penicillin. If the latter is administered, I think that 20,000 units should be given every three hours around the clock for one week.

DR DAVID BLOOM. The edema may be assumed to have developed on the basis of the long-standing eczema of the hands. At present it is not associated with any inflammatory sign, and I therefore do not expect any benefit from sulfonamide compounds or penicillin.

## NEW ENGLAND DERMATOLOGICAL SOCIETY

JACOB H SWARTZ, M D, *President*

FRANCIS M THURMON, M D, *Secretary*

*Boston, Oct 18, 1944*

**Chronic Lymphangitis of the Lower Lip** Presented by DR J H SWARTZ, Boston

J M, a white American school girl aged 9, presents an intermittent swelling of the lower lip, of eight years' duration.

During this period the lip has never been entirely normal. At the onset there were edema and vesiculation, but during the past two years the edema has persisted without vesiculation.

Examination reveals a firm swelling of the lower lip, without tenderness.

The Hinton and Wassermann reactions of the blood were negative.



Autogenous, typhoid and smallpox vaccines have been administered Moccasin snake venom, as well as roentgen therapy totaling 450 r, has been used No improvement resulted from this treatment

## DISCUSSION

DR F P McCARTHY, Boston I have a patient with a similar condition of three years' duration, who was treated elsewhere for about one year and received essentially the same therapy as that recorded here, exclusive of roentgen rays but including a sulfonamide compound and a streptococcus vaccine My patient has periodic attacks of fever at intervals of two to three weeks, the edema being severe and even intraoral, and similar to that of the patient shown today I have given solution of potassium arsenate U S P, a high vitamin intake and small doses of roentgen rays All her teeth have been extracted Over a period of six months the lymphedema has diminished about 50 per cent

DR J H SWARTZ, Boston This patient states that she does not feel well at times, especially when the "blisters" erupt

DR F P McCARTHY, Boston The patient of mine also has chronic aphthous stomatitis

DR F RONCHESI, Providence, R I Did you use an intraoral apparatus for the roentgen ray therapy?

DR G M CRAWFORD, Brookline, Mass I did not happen to see her during roentgen treatments, but I am sure that she had a shield on the inside of the lip My colleagues and I have no oral unit

DR J H SWARTZ, Boston The problem in this case is not only the diagnosis but the question of what to do I recall a member of my own family who had a similar lymphedema for a period of years and received all forms of therapy, with only temporary improvement The only thing that did him good was plastic surgical treatment He had involvement of the lower lip chiefly and some of the upper lip There has been no recurrence since about twelve years ago

DR B APPEL, Lynn, Mass What was done surgically?

DR J H SWARTZ, Boston I am sorry that I cannot describe the technic The operation was done by a good plastic surgeon, with an excellent result

DR J GOODMAN, Boston When penicillin was first available, I was presented with a patient who had the same disease that has just been described The duration was seven or eight years The process was on the cheeks It was characterized by recurrent episodes of fever, redness and induration of the cheek and sometimes enlarged lymph nodes of the neck The patient had received roentgen ray therapy At that time she was taking sulfathiazole, and she had been taking it for a year Whenever fever developed she would take sulfathiazole for a few days, and the fever and edema would subside I administered penicillin, a total of 300,000 units within three days The process quieted down while she was in the hospital A week after her discharge it disappeared entirely, and there has been no recurrence However, the patient has had similar episodes of freedom from attacks

DR F P McCARTHY, Boston Is there any lymphedema between attacks?

DR J GOODMAN, Boston There is not

#### A Case for Diagnosis (Dermatitis Repens?) Presented by DR WALTER F LEVER, Boston

T B, a white American woman aged 44, presents a lesion on the left thumb of eight years' duration

Subsequent to the removal of a wart, the lesion developed, and it has persisted on the dorsal surface of the left thumb The area has remained almost constant in appearance, in spite of many types of therapy It has never healed entirely,

and at times deep pustulation has been present. It has been slightly tender and does not itch.

The examination reveals an eroded erythematous scaling area, approximately 2 cm in diameter, on the dorsum of the left thumb.

The Hinton reaction of the blood on two occasions has been negative. No foreign body or osteomyelitis was seen on roentgenologic examination. Cultures yielded abundant *Staphylococcus aureus* organisms.

Treatment has comprised numerous bland ointments and compresses and application of 1 per cent aqueous solution of basic fuchsin. Sulfathiazole ointment and sulfapyridine orally were used and sensitivity to these sulfonamide compounds developed within five days. An occlusive dressing was applied for five weeks to rule out dermatitis factitia. Seven injections of staphylococcus toxoid were given. Despite this therapy, the lesion has persisted.

#### DISCUSSION

DR. F. P. MCCARTHY, Boston. This patient is a confirmed picker and admits past and present picking at the lesion.

DR. J. H. BLAISDELL, Boston. It seems to me that this case raises a simple and practical question in dermatology. Is it consistent with dermatologic thought that an area of dermatitis may remain as small as a half-dollar for a period of eight continuous years?

DR. W. F. LEVER, Boston. I did not make the diagnosis of dermatitis repens but only raised the question of the presence of this disease, that seemed to be the closest diagnosis that could be established. The possibility of dermatitis factitia has been considered. The patient admits picking, but it is not quite the type of lesion that I should expect to result from picking alone. I thought that bacterial infection was somewhat involved in the production of the lesion and thought that bacterial dermatitis might be considered. On the whole, I am uncertain about the diagnosis.

#### **Poikiloderma Vasculare Atrophicans** Presented by DR. G. MARSHALL CRAWFORD, Brookline, Mass.

G. G., a white American man aged 49, presents lesions on the trunk and extremities of fifteen years' duration.

After seven months in the tropics, he observed red areas on the trunk, some of which have slightly enlarged and others of which have receded. There has been no appreciable pruritus. There is no other relevant anamnesis.

Examination reveals irregular scattered lesions on the trunk and extremities. The areas are sharply defined and of varying shapes, some are as large as 10 cm in diameter. Atrophy, pigmentation and varying degrees of telangiectasia are present. A few of the areas show mild scaling.

The Hinton reaction of the blood was negative. Cultures yielded *Staphylococcus albus*.

The patient has not been treated.

#### DISCUSSION

DR. J. G. DOWNING, Boston. This case is not a true picture of poikiloderma vasculare atrophicans. One or two plaques showed evidence of dilatation of the capillaries. When the lesion on the back, an elevated circular plaque with numerous dilated capillaries, undergoes involution, there will be residual capillary dilatation similar to that which he presents on the medial aspect of the thighs. I think that this picture suggests an eruption of the parapsoriasis type rather than poikiloderma.

DR. J. H. SWARTZ, Boston. I favor the diagnosis of psoriasis. Here is a man with a dermatitis of fourteen to fifteen years' duration, with scaling, erythematous patches, little atrophy and little capillary dilatation which accom-

panies poikiloderma vasculare atrophicans The slightly infiltrated lesion on the back suggests premycosis fungoides, even though the dermatosis is of fourteen or fifteen years' duration I recall a similar case of twenty years' duration, with itching for a number of years, which terminated as a case of typical mycosis fungoides

DR G M CRAWFORD, Brookline, Mass The suggestion is certainly appropriate This man came to me only because his local physician was curious as to the nature of his eruption He was unconcerned with it because it did not bother him It became apparent while he was in the tropics The one elevated lesion is distinct from the others I cultured that mainly to rule out a fungous infection He would not consent to a biopsy At the time I saw him, there was no scale on any of the lesions except that thickened plaque Some of the older areas showed a good deal of atrophy They are inconspicuous and not as pigmented as they should be

**Keratosis Palmaris et Plantaris (Due to Arsenic)** Presented by DR WALTER F LEVER, Boston

E C, an Italian man aged 44, presents keratotic lesions on the palms and soles which are of approximately one year's duration

In June 1941 an eruption developed which was diagnosed as dermatitis herpetiformis In January 1942 solution of potassium arsenite U S P, 30 cc, was prescribed by his local physician Up to December of that year, the patient had refilled this prescription on four occasions In October 1943, numerous keratotic lesions began to appear on the palms and soles

DISCUSSION

DR W P BOARDMAN, Boston I think that this is a typical case of palmar and plantar keratosis

DR W F LEVER, Boston I should like to point out that in this case the patient was given by his physician a prescription for 30 cc of solution potassium arsenite On four occasions the patient refilled the prescription without the knowledge of any physician Only when the fifth refill was requested was it suggested by the pharmacist that he see his physician

DR B APPEL, Lynn, Mass As long as the discussion has gone off on this tangent, I think that I might mention my own custom in writing a prescription for medicines which might cause damage by constant refilling I am extremely careful always to note on the prescription that use of the preparation should not be repeated, and the druggists to my knowledge have never refilled such a prescription It seems to me that physicians, above all, who know the dangers of their medicines, should exercise care For instance, I had several patients who were taking sulfapyridine Although physicians are well aware of the lack of its apparent toxic effect, I nevertheless write every prescription for an amount of tablets which I know is appropriate at that visit and signify that it should not be refilled I do the same for thyroid tablets, and, although I have seldom used solution of potassium arsenite, I always write *non repetatur* on the prescription I respectfully recommend that as a standard procedure for all who write prescriptions

DR G A DIX, Worcester, Mass In Worcester, the patients have a habit of asking for a copy of the prescription It is sometimes advisable to say, "Do not refill or give a copy"

DR J H BLAISDELL, Boston How many ounces of solution of potassium arsenite did this man take?

DR W F LEVER, Boston One hundred and fifty cubic centimeters

DR J H BLAISDELL, Boston The only thing that interests me is that this man had 2,500 minims (154 cm) at his disposal, and he took it over a period of

ten months. Now if he took in on an average of 15 drops a day, it would be for a period of one hundred and fifty days only. Otherwise, he did not take an excessive amount, but he had an idiosyncrasy to arsenic.

#### **Tuberous Sclerosis** Presented by DR J H SWARTZ, Boston

L P, a white American school boy aged 17, presents lesions of thirteen years' duration involving the face, trunk and nails.

There have been an eruption on the face and moles over various parts of the body since the age of 5 years. Deformity of the nails with fibromatous changes has been present as long as the patient can remember, and this has been attributed to his biting his nails. The patient has been retarded mentally and has had convulsions for the past three years.

The clinical picture is that of typical adenoma sebaceum of the face. There are multiple moles on the trunk, and the nails are deformed. Neurologic examination reveals, aside from the convulsions and loss of consciousness, a bilateral Babinski sign but otherwise generally normal reflexes. Profuse perspiration is noted.

On roentgenologic examination the skull was normal. The Hinton reaction of the blood was negative. The leukocyte count was 13,600. Urinalyses were irrelevant except that the test for sugar with Benedict's solution showed green on two occasions. The nonprotein nitrogen was 38 mg per hundred cubic centimeters. An electroencephalogram was reported as "a grossly abnormal record. It showed a diffuse, high voltage, slow wave dysrhythmia which was increased by overbreathing. It showed a focus in the right occiput. The focus was so pronounced as to make one suspect that the patient has a tumor. He merits localization study with sixteen scalp electrodes."

#### DISCUSSION

DR F RONCHESE, Providence, R I: What pathologic change, other than that resulting from nail biting, is there in the nail?

DR J H SWARTZ, Boston: Sometimes the patient says that the nail became changed after he bit it, but the mother reports that he began to bite the nail after the change in the nail was called to his attention. This type of involvement of the nails has been described in cases of tuberous sclerosis.

DR L BABALIAN, Portland, Maine: Subungual and periungual fibromas have been described in tuberous sclerosis. I wonder whether they could be considered in this case.

DR J H SWARTZ, Boston: He has one lesion which is fibromatous extending to the nail.

DR F RONCHESE, Providence, R I: He claimed that he had an accident to that nail.

DR G E MORRIS, Boston: Since this patient presents mental deficiency, epilepsy and tuberous sclerosis, the disease might fall into the category of epiloia, which is an enlargement of the idea of tuberous sclerosis to include associated medical findings.

#### **Lipid Proteinosis, Generalized** Presented by DR G MARSHALL CRAWFORD, Brookline, Mass

J S, a white American man aged 28, presents a generalized dermatosis of twenty-three years' duration. When the patient was 5 years old, lesions began to appear on the face, scalp, trunk and extremities, which were attributed to "infections." They appeared in crops one or more times yearly, requiring months to heal, and scarring was always pronounced. There was a remission of lesions during the "teen age period," but since that time he has had several severe episodes, involving especially the scrotum and buttocks. There was a question-

able family history of diabetes. In recent years the patient suffered "fainting spells" of an epileptiform type, which were not controlled by diphenylhydantoin sodium.

Nearly all the skin is of ivory or yellowish color of varying degrees, except for the areas of severe scarring. The scars vary in size, many are atrophic and others varioliform, and they are most evident on the face and the scrotum. Myriads of yellowish white milium papules are present on the face, neck and eyelids, especially at the margins of the eyelids. Hypertrophic changes are present on the knees, elbows and buttocks. There are milium lesions on the oral and nasal mucous membrane. Several teeth are missing, possibly some congenitally. The maxillary canine teeth are sharply pointed. There are deformities of the enamel. Irregular thickening of the vocal cords is noted.

The Hinton and Wassermann reactions of the blood were repeatedly negative. The results of an examination of the blood and urine were normal. The blood cholesterol level in 1938 was 151 mg per hundred cubic centimeters and 235 mg in 1944. The nonprotein nitrogen was 20 mg, chlorides 106 mg, total protein 6.8 Gm and blood sugar 82 mg per hundred cubic centimeters. Roentgenologic examination of the long bones showed that they were normal, and calcification of the tentorium was noted in the skull. The cerebrospinal fluid was normal. An electroencephalogram suggested brain tumor. A biopsy in 1938 showed normal elastic tissue, but the central arteriole of each papilla showed a uniform coat of fat forming a sheath about the blood vessel.

#### DISCUSSION

DR J. H. SWARTZ, Boston: This is an interesting and rare case. The lesions around the eyelid are yellowish and characteristic of lipid proteinosis. I want to congratulate Dr. Crawford in being the first to make the diagnosis. I made the diagnosis independently and later found that Dr. Crawford already had established it. The case is well worth reporting.

DR G. M. CRAWFORD, Brookline, Mass.: That is a bit of a reflection on all of us. This man was in my ward at the Massachusetts General Hospital in 1938 with a diagnosis of epidermolysis bullosa. The most interesting feature of this particular case is the possibility of cerebral involvement. His mental hallucinations began only during the last ten years, and his fainting spells, which finally became definite grand mal, some of them violent exhibitions, occurred only within the past five years. The electroencephalogram indicates a possible tumor. So far, that has not been reported among 22 previously recorded cases. This man is on the waiting list to go to Monson State Hospital, Palmer, Mass. If he dies there, it will probably be possible to get an autopsy. I do not know when that will be, but I do not predict any great length of life for him.

#### A Case for Diagnosis (Sarcoidosis of the Cheeks and Forehead, Tuberculosis Luposa?) Presented by DR. WALTER F. LEVER, Boston

I. G., a French housewife aged 49, presents lesions of ten years' duration on the cheeks and forehead. The presenting lesions gradually have increased in size and number over the past ten years. During the winter of 1943-1944, the patient felt weak and tired and had two small hemoptyses. At present she has paroxysms of coughing each morning.

Examination reveals sharply demarcated, raised, slightly infiltrated lesions of purplish color on the cheeks and forehead. On percussion there is dullness over the base of the right lung anteriorly and posteriorly. The voice sounds and fremitus are diminished over the base of each lung. There are cavernous breath sounds, both anteriorly and posteriorly, at the base of the left lung.

The results of the tuberculin test (dilutions of 1:100,000 to 1:1,000) were negative. Roentgen examination of the lungs revealed a partial collapse and consolidation of the middle lobe and a linear infiltration of both lower lobes. A cutaneous biopsy showed numerous sharply demarcated islands of epithelioid cells.

in the corium and lymphocytes both around and within the islands. A decision as to whether or not the process was sarcoid or lupus vulgaris could not be made from the section.

#### DISCUSSION

DR B APPEL, Lynn, Mass. Diascopic pressure revealed "apple jelly" nodules varying from 1 mm to 5 mm in diameter, which with the generalized structure and distribution of the lesions indicates tuberculosis luposa (*lupus vulgaris*).

DR G M CRAWFORD, Brookline, Mass. I do not recall whether a guinea pig has been inoculated.

DR W F LEVER, Boston. A guinea pig has been inoculated, but insufficient time has elapsed for a report.

DR G M CRAWFORD, Brookline, Mass. That will have to determine the diagnosis, since the pathologic changes are not clear.

DR A HOLLANDER, Springfield, Mass. I suggest the diagnosis of sarcoid especially because of the whitish discoloration of the periphery of the lesions. I should not say that this is a typical case of tuberculosis luposa (*lupus vulgaris*).

DR J GOODMAN, Brookline, Mass. I favor the diagnosis of sarcoid. One cannot be sure of the guinea pig inoculation, but I am inclined from the clinical observations to make a diagnosis of sarcoid.

DR W P BOARDMAN, Boston. The pinkish color, soft consistency and circular contour of the lesion suggests gumma, and had it broken down I should have called it a gumma. I could not find any nodules. I thought it was sarcoid. It is unusual to have *lupus vulgaris* start at that age. Similar cases of tuberculosis luposa in adults have been presented to the society, but they certainly are unusual.

DR J G DOWNING, Boston. Smears for Hansen's bacilli should be made.

DR M RYAN, Brockton, Mass. She has a lesion on the knee which looked like sarcoid.

DR J H SWARTZ, Boston. Have smears for Hansen's bacillus been made?

DR W F LEVER, Boston. The Ziehl-Neelsen stains were negative. Roentgen studies of the chest showed massive consolidation of the middle lobe of the right lung and the lower lobes of both lungs. This is in favor of sarcoid. Furthermore, the striking contrast between the massive infiltration of the lungs and the lack of impairment of the general health favors sarcoid. All tuberculin tests elicited negative reactions. As far as the histologic examination is concerned, the slide was shown to Dr Max Pinner, of the Montefiore Hospital for chronic diseases, in New York, and he felt that the diagnosis was not sarcoid, but in the pathologic laboratory at the Massachusetts General Hospital the consensus was sarcoid.

#### Giant Cell Reticulosis. Presented by DR WALTER F LEVER, Boston

J P, a white American man aged 45, complained of a nonitching eruption of two years' duration. The onset was marked by a dry, erythematous, nonpruritic scaling on the lower half of the abdomen, extending to the groins and thighs. Later the axillae and the right popliteal space were similarly involved. Seven months ago, painless hard subcutaneous masses began to develop in and about the erythematous areas and also appeared beneath the left nipple and on the lower portion of the back. Fatigue has been noted for the past six months.

The erythematous areas blanched on pressure and were slightly warmer than the surrounding skin. Painless, firm masses, which tended to be confluent and slightly elevated, ranging from 1 to 5 cm in diameter, were seen on the medial and lateral aspects of both thighs, the groins and the lower portion of the back. Three yellowish colored elevated masses were noted beneath the left nipple.

Six biopsies were performed, and histologic studies revealed reticulum cells interspersed with giant cells showing asteroid inclusion bodies. The blood showed a hemoglobin content of 78 per cent (Sahli), an erythrocyte count of 4,100,000 and a leukocyte count of 4,900, the differential count was normal. On examina-

tion the urine was normal. The blood cholesterol level was 195 mg per hundred cubic centimeters. The nonprotein nitrogen was 37 mg and the second determination 30 mg per hundred cubic centimeters. The total protein content was 6.18 Gm, albumin 3.94 Gm and globulin 2.24 Gm per hundred cubic centimeters (albumin globulin ratio 1.7:1). There was a positive reaction for urobilinogen in the 1:80 dilution and a negative reaction in the 1:160 dilution. The prothrombin time was twenty-two seconds. There was no reaction to tuberculin in a dilution of 1:10,000. Roentgenologic examination of the heart and lungs showed normal conditions. Results of the glucose tolerance test were as follows:

	Sugar in Blood, Mg /100 Cc	Sugar in Urine (Reduction of Benedict's Solution)
Fasting	94	Negative
Half hour	125	Negative
One hour	125	Negative
Two hours	125	Negative
Three hours	102	Negative
Four hours	63	Negative

Determination of the total lipids in the blood resulted as follows:

	Blood	Plasma	Cells
Leclithin, Mg /100 Cc	276	213	353
Cholesterol, Mg /100 Cc	195	210	182
Cholesterol esters, Mg /100 Cc	83	127	29
Total fats, Eq /l	17.3	18.1	16.4
Neutral fats, Fq /l	8.5	9.9	7.4

#### DISCUSSION

DR. W. F. LEVER, Boston: The sections were studied here in the pathologic laboratory, and nobody seemed to be sure about the nature of the lesions. I took the sections to Dr. S. Burt Wolbach, professor of pathology of Harvard Medical School, and it turned out that he had first described a similar type of lesion in 1911 (Wolbach, S. B. A New Type of Cell Inclusion, Not Parasitic, Associated with Disseminated Granulomatous Lesions, *J. Med. Research* 24:243, 1911). He had described the star-shaped inclusion bodies, which are present in the giant cells of this lesion. Their significance is not known. The histologic slide in this case shows groups of reticulocytes and large multinuclear cells embedded in bands of fibrosis. The histologic diagnosis of giant cell histiocytic reticulosis was first applied to this type of lesion by Robb-Smith of England (Robb-Smith, A. H. T. Reticulosis and Reticulosarcoma, *J. Path. & Bact.* 47:457 [Nov.] 1938). Wolbach found these lesions in the lung, spleen and lymph nodes of 4 patients who had died from other diseases. They were found accidentally. Dr. Wolbach told me that the sections in the present case did not suggest lymphoma but suggested rather a non-bacterial granuloma. Although he could not compare it with another type of lesion, he thought that the lesion belonged in the same group with sarcoid and the nodules found in rheumatoid arthritis.

DR. F. P. MCCARTHY, Boston: Does this patient have an enlarged spleen?

DR. J. G. DOWNING, Boston: Have any cases been reported of lesions appearing on the skin?

DR. W. F. LEVER, Boston: None have ever been reported.

DR. J. H. SWARTZ, Boston: I read Dr. Wolbach's article just cited by Dr. Lever, and, to judge from the description, the lesions were miliary, whereas those in this case are large-sized tumors. One would immediately think of a possible lymphoma or a mycosis fungoides prior to breaking down. One tumor has a yellowish color, as Dr. Crawford remarked, and this suggests xanthoma. I predict that this patient will show a lymphoma, in spite of the fact that the present pathologic picture is not characteristic of that entity.

**A Case for Diagnosis (Lymphoma, Furunculosis?)** Presented by Dr G MARSHALL CRAWFORD, Brookline, Mass

H M, a white Canadian farmer aged 58, presents a generalized eruption of three and a half years' duration. At the onset, after exposure to "Crystal Dip" (phenol base), an edematous, papular, erythematous burning and pruritic eruption developed over the exposed portion of the patient's face, neck and arms. At that time, his local physician administered ten semiweekly treatments of poison ivy extract, after which the eruption became generalized. Approximately eighteen months ago, large, painless and transient subcutaneous masses began to develop, some of which recently have suppurated and drained. The patient complains chiefly of the pruritus and an unusual feeling of warmth.

Examination reveals a generalized thickening of the skin of the forearms and legs. Subcutaneous masses, 4 cm in diameter, are present on the medial portion of the right thigh, in the right inguinal region and on the chest and forearms. Furunculosis involves the occiput. The patient also presents hyperthyroidism and coronary heart disease with moderate decompensation.

A leukocytosis with a count of about 14,000, and an eosinophilia, with a content of 14 to 28 per cent, persisted. Occasional casts and traces of albumin were present in the urine. The glucose tolerance test showed a level of 161 mg per hundred cubic centimeters after two hours. The prothrombin time was twenty-seven seconds. Cultures from lesions on the right groin and back yielded *Staphylococcus aureus* and beta hemolytic streptococci. Thus far, treatment has comprised bland soothing applications.

## DISCUSSION

DR W P BOARDMAN, Boston. Was the spleen enlarged? I found a few enlarged lymph nodes.

DR J H SWARTZ, Boston. Dr Luikhart, you examined the patient carefully. Did he have an enlarged spleen?

DR R LUIKHART. He has no enlargement of the spleen or liver.

DR W P BOARDMAN, Boston. I could not help thinking of a lymphocytic leukemia. There is not much on which to base my opinion except the lymphocytosis.

DR J H SWARTZ, Boston. I remember seeing the slide. I thought it showed in one area a picture suggestive of lymphoma.

DR W F LEVER, Boston. After the first biopsy, a slide from which was presented, a second one was made of the skin and lymph nodes. The lymph nodes were normal, but the section of skin showed unusual changes in the subcutaneous fat, mainly in and around the blood vessels. Dr Benjamin Castleman thought that the changes were consistent with periarteritis nodosa. He mentioned, however, that these lesions of periarteritis nodosa were not specific and that similar changes could occur in other diseases.

DR J G DOWNING, Boston. I never thought of periarteritis nodosa in relation to this case.

DR G E MORRIS, Boston. Was there ever any oozing from the man's lesions? I thought that it was a classic picture of chronic exudative discoid and lichenoid dermatitis described by Sulzberger and Garbe in 1937.

DR J H SWARTZ, Boston. None of the lesions have been vesicular, and the genitals have not been involved.

**Lupus Erythematosus** Presented by DR ROBERT H GOLDFARB, Boston

G Z, a Russian Jewess aged 50, presents lesions on the face of five years' duration.

Examination reveals erythematous patches with atrophy and follicular plugging about the eyes, nose and premalar areas.



The Hinton, Wassermann and Kahn reactions of the blood were negative. Roentgenologic examination of the bones of the cheeks showed nothing abnormal. Treatment has comprised injection of gold sodium thiosulfate intravenously in 10 mg doses, which was discontinued because of nausea, and of bismuth subsalicylate intramuscularly, without improvement.

## DISCUSSION

DR J H BLAISDELL, Boston: Has any one had any experience in giving strong solution of iodine U S P? Dr Benson Cannon, of New York, reported a small number of cases before the American Dermatological Association in which there was a definite improvement from giving a small amount of strong solution of iodine.

DR J H SWARTZ, Boston: This happens to be 1 case in which I gave potassium iodide instead of strong solution of iodine. I saw the patient before she went to the Boston Dispensary, and at that time there was pronounced lymphedema. I did not see her again until today. I do not know that she took the potassium iodide.

DR R H GOLDFARB, Boston: We tried to get some information as to the past treatment, but she refused to talk except to say that she had been to several good dermatologists.

DR C S SAWYER, Boston: I have not tried strong solution of iodine but have given potassium iodide to several patients with lupus erythematosus, without noticeable benefit.

DR J H BLAISDELL, Boston: Dr Cannon reported that potassium iodide was not particularly effective but that the more effective strong solution of iodine contains 5 per cent elemental iodine and 10 per cent potassium iodide in aqueous solution. It was given in doses of 3 to 5 minims (0.18 to 0.31 cc) three to five times daily.

DR J G DOWNING, Boston: Has anybody made a diagnosis of the mass on the left zygoma?

DR J H SWARTZ, Boston: Roentgenologic studies showed that the left zygoma was normal. I had a surgeon see her, and he felt that the swelling was due to lymphatic obstruction.

### Psoriasis Presented by DR BERNARD APPEL, Lynn, Mass

R D, a Rumanian woman aged 45, presents lesions of the mucocutaneous junction of the lips, of four years' duration. In August 1940, typical psoriasis of the elbows was seen, together with scaling of the vermilion border of the lips. At that time patch tests with lipstick, nail polish and tooth powder which she used elicited negative reactions. Treatment comprised nicotinamide given orally and a coal tar ointment administered locally, with improvement. Three months later there was an exacerbation of lesions of the lips and the elbows. Ultraviolet radiation was administered, with benefit. In March 1944, there was an acute dissemination of the psoriasis and a recurrence of the patchy scaling lesions of the lips. Despite treatment the lesions of the lips and the psoriasis of the knees have persisted.

Examination reveals a thin reddish purple line of fine white scales at the junction of the mucous membrane and skin of the lips. There are thin, silvery scaling, dry infiltrated plaques on the elbows and knees, together with a few scattered papules on the thighs and insteps. Punctate bleeding points can be demonstrated in the lesions.

The Hinton reaction of the blood was negative.

## DISCUSSION

DR G M CRAWFORD, Brookline, Mass: So far, I have never been convinced that psoriasis occurs on the mucous membrane. There is always a first time,

and this may be it. In this case, because of the primary lesion, the scaling of the lips and the psoriasis on the elbow, I favor a diagnosis of cheilitis exfoliativa to account for the lesions on the lip, in the absence of any other cutaneous lesion I think a biopsy should be performed.

DR J H SWARTZ, Boston. I am inclined to feel that Dr Appel was correct in his diagnosis. There is a sharp border of erythema and scaling. By covering the lip and looking at the periphery, one would say that it is psoriasis. The patient had lesions on the buccal mucous membrane, which I should like to include in the diagnosis of psoriasis. It is the first case in my experience which I should call psoriasis of the lip and buccal mucosa.

DR F P MCCARTHY, Boston. I might say that I have been looking for psoriasis in the oral cavity and mucous membranes for twenty years, and this case is the most suggestive to date.

DR B APPEL, Lynn, Mass. I am flattered to have an agreement with my diagnosis. If my memory serves me correctly, when I showed this patient before this society two years ago Dr McCarthy's comments were almost identical with those of today except that today he reluctantly added that the diagnosis of psoriasis might be correct. When I first saw this patient, a diagnosis of psoriasis of the lips was made with hesitation. At that time she had lesions only on the lips. My colleagues did not believe that it could be psoriasis, yet I, for that very reason, maintained it was psoriasis. Much to my surprise, psoriatic lesions developed elsewhere, and I now am glad to see that my original diagnosis has been confirmed. It is my first case of psoriasis of the lips. I shall probably not be able to perform a biopsy.

#### **A Case for Diagnosis (Lichen Planus?)** Presented by DR JOSEPH GOODMAN, Boston

R W., a white boy aged 7, presents vesiculation and bullous lesions on the arms, legs and V of the neck of five weeks' duration. The onset was marked by the sudden appearance of pruritic vesicles on the arms, legs and chest. These lesions have persisted in the originally involved areas, without extension.

Examination reveals sharply outlined bluish red and erythematous scaling papules, both discrete and grouped over the aforementioned areas. On the arms there are several flaccid bullous lesions within the red scaling areas, and some of these bullae are hemorrhagic.

The hemoglobin content was 76 per cent (Sahl), the erythrocyte count 4,150,000 and the leukocyte count 6,900. Examination of the urine revealed nothing abnormal.

Treatment has comprised topical applications of paste of zinc oxide and calamine lotion, without apparent improvement.

#### DISCUSSION

DR J H BLAISDELL, Boston. I do not believe that this is lichen planus bullosus. The child gives a history of acute dermatitis starting on the legs and arms, which followed an application of two ointments. I should say that it is a contact dermatitis.

DR J H SWARTZ, Boston. I agree with Dr Blaisdell. This is a contact dermatitis. There were lichenoid lesions in some areas, but they were not of the pattern which one customarily sees in lichen planus. For a child, the diagnosis of lichen planus should be made with reservation. I suggest that a biopsy be performed.

DR J GOODMAN, Boston. When I first saw this patient and again at the time of the second visit, there were five or six good-sized bullous lesions, which have disappeared. I felt that this was probably not a contact dermatitis because of the sharp outline of the lesions and the infiltration of certain lesions and also because

at the time of his second visit there had been a lack of improvement with simple treatment. I have not been able to offer a proper diagnosis.

**Acrodermatitis Atrophicans Chronica** Presented by DR JOSEPH MULLER, Worcester, Mass

M. S., a white woman aged 67, presents lesions on the arms and legs of ten years' duration.

At the onset she noticed that the legs were bluishly discolored, and on the legs there were open ulcers, especially during the summer months. Last winter the skin of the left elbow and forearm became red and swollen, and for the past month a similar change has been noted on the right forearm. She complained of itching of the lower extremities. The thighs and legs presented a thin tissue-paper-like, dry furfuraceous desquamation and a loss of subcutaneous tissue.

The skin of the radial side of the right forearm is red, and an elongated tumor is palpable in the center of this area. There is a similar but less extensive involvement of the right elbow. The skin elsewhere appears to be normal.

The Hinton reaction of the blood was negative.

DISCUSSION

DR W. F. LEVER, Boston: I was impressed with the induration of the lesions located on the dorsa of the feet and distal to the elbows. They had the character of scleroderma.

DR J. MULLER, Worcester, Mass.: The discussion of scleroderma and acrodermatitis atrophicans is an old one. That started in the eighties, before you and I were existent, but I do not think that there is anything characteristic of scleroderma in the coloration of the skin in this case. It is interesting to look carefully at the tumor-like structure and note that the skin can be moved over the mass. The tumor is entirely in the subcutaneous tissue. I should like to get a biopsy of this tumor, but permission cannot be obtained.

DR G. E. MORRIS, Boston: I agree with the diagnosis of acrodermatitis. Since it is more common in women, I should try some treatment with male sex hormones for this patient.

**Tinea Capitis in an Adult** Presented by DR JOSEPH M. GOODMAN, Boston

J. T., a white American housewife aged 38, presents an infection of the scalp of seven weeks' duration. At the onset there was an itching bald area on the crown of the scalp. Her children showed no involvement of the scalp, but their arms, legs and faces had transient, red scaling lesions.

Examination reveals a scaling area 4 cm. in diameter on the crown where the hairs are scattered and broken off. Anterior to this lesion the scalp presents a slight scaling without appreciable loss of hair. On illumination of the involved portion with a Wood filter there is fluorescence of the hairs.

The Hinton reaction of the blood was negative. Microscopic examination of the hairs from the affected portion of the scalp showed many spores surrounding the hairs and mycelium within the hairs. Cultures from the lesion yielded *Microsporon lanosum*.

The area has been treated with sulfur and salicylic acid ointment, without favorable change.

DISCUSSION

DR E. M. ROCKWOOD, Boston: That is the first case of tinea capitis of the *Microsporon lanosum* type I have seen in an adult.

DR J. H. SWARTZ, Boston: I was hoping against hope to prove the diagnosis wrong, because the lesion appeared to be an alopecia areata which had been over-treated, thus producing scaling and loss of hair. There was an absence of inflammatory reaction in that area. I epilated hairs and found that they were broken and surrounded by a white sheath. Under the microscope the hairs were filled

with spores. On culture mounts there were present these beautiful, large spindle-shaped fuseaux. The mother stated that her child had lesions on the glabrous skin. There are a dog and a cat in the house, but the mother did not know whether they had lesions. I think that it is an interesting and rare case.

DR G. SCHWARTZ, Boston. Three or four years ago there was a nurse in charge of a pediatric ward in one of the Boston hospitals, and she had a tinea capitis which was proved by culture.

DR G. E. MORRIS, Boston. Since the use of endocrine products in the treatment of mycotic infections has been reported, it might be a good idea to have an endocrinologist see her. This woman might have a prepuberty type of endocrine swing.

DR J. GOODMAN, Boston. I have not had an opportunity to examine this woman's four children. I did see one child, but I did not take a culture of scrapings. The lesions appeared suspicious. To listen to the patient, one would think that in her town there is a raging epidemic of fungous infection. I was surprised when I examined this patient's scalp with the Wood filter. Not only were there fluorescent hairs in the area of involvement, but also there were many small normal-appearing areas in which there were fluorescent hairs. I too, on first sight, felt that this was alopecia areata which was overtreated and was therefore scaling. The evidence is complete that this is a *Microsporon canis* infection.

**Stomatitis.** Presented by DR FRANCIS P. MCCARTHY, Boston.

R. B., a white man aged 46, presents lesions of the mouth, of six months' duration. In April 1944, sulfonamide drugs were administered for pneumonia, and at this time painful exudative lesions developed beneath his upper denture. These lesions gradually spread to involve the buccal mucosa of the entire mouth. His local physician administered further sulfonamide drugs, various mouth washes including sodium perborate and arsphenamine, together with topical applications of gentian violet medicinal. At the present time there is little soreness of the mouth but there is increased exudate in the morning.

Examination reveals edematous exudative erosions 2 mm in diameter with fairly symmetric distribution involving the hard and soft palate, gums and buccal mucosa. The mucosa appears exuberant, especially in the molar regions.

Bacteriologic studies yield aerobic, anaerobic and mycotic organisms, but no virus could be demonstrated. Roentgenologic studies of the chest gave normal results. A biopsy showed a nonspecific inflammatory reaction. Serologic tests for syphilis were negative.

Irrigations with isotonic solution of sodium chloride each morning reduce the oral exudate for a twelve hour period. Six capsules of Polytavin (each containing 10,000 U. S. P. units of vitamin A, 0.45 mg. of thiamine hydrochloride, 50 micrograms of riboflavin, 25 mg. of ascorbic acid and 1,000 U. S. P. units of crystalline vitamin D, from ergosterol) have been taken daily, which probably accounts for some of the improvement, although the process is now stationary.

#### DISCUSSION

DR J. G. DOWNING, Boston. The patient has decided hypertrophy of the glands and gives a history of having, on awakening, a sticky discharge from the labial mucous membrane. I believe that this is a case of hypertrophy of the mucous glands of the mouth plus an additional stomatitis. The stomatitis may be due to secondary infection.

DR F. P. MCCARTHY, Boston. This is 1 of 2 identical cases. The man presented today has an edentulous mouth, while the other patient, a woman aged 26, has a fair set of teeth. The stomatitis of the woman followed an attack of meningitis and pneumonia which occurred a year prior to the eruption in her mouth. The oral lesions in both cases were symmetric and started from a localized area. In the case of the woman, on the right upper gingiva, in the case of the man, on the palate. In both cases at the onset the process was vegetative in character and suggested a lupus reaction. There were edema, exudate, a fetid odor to the

breath and only slight subjective symptoms to go with the oral lesion. The general health has remained good. The man had two months of fever in the early stages of his oral eruption. The woman was given penicillin for five days. She also had sulfathiazole for a short period, without improvement. They both had gentian violet medicinal administered locally. Serologic reactions for syphilis were negative. They received vitamins and numerous local applications, including arsphenamine. Biopsy specimens from both patients showed intact stratified squamous epithelial surfaces. The cells showed edema with many vacuoles. There was a cellular infiltration of the upper part of the cutis, the cells being pleomorphic in character, with numerous eosinophils. Attempts to isolate a virus from the sputum were unsuccessful. The 2 cases are rather extraordinary in that each patient received sulfonamide compounds for pneumonia. The sulfonamide drug may have precipitated the stomatitis, while oral micro-organisms became secondary invaders. I do not believe that a definite diagnosis can be made in these cases. They suggest a chronic stomatitis with secondary infection in persons who previously had debilitating diseases for which sulfonamide compounds were used.

DR J G DOWLING, Boston. Would you consider in either of these 2 cases the possibility of the patient's having had originally an infectious mononucleosis?

DR F P MCCARTHY, Boston. Normal blood counts were obtained early in both cases. In the case of the man presented today with the afternoon fever, I thought of undulant fever or tuberculosis. The roentgenograms of the chest were normal, and the lymphocyte count was not elevated. There was no enlargement of the spleen. I ruled out cheilitis glandularis aspostematosa because that disease is confined to the lips and represents a congenital hyperplasia of the mucous glands in the lips.

**Lichen Planus Hypertrophicus** Presented by DR BERNARD APPEL, Lynn, Mass. A P, a Negro man aged 40, presents lesions on the lateral and anterior aspects of the legs of eight years' duration. The onset was marked by lesions appearing in the scars resulting from burns. Following topical medication, "blisters" appeared in ringlike formation. Pruritus was intense. Six months later a dark pigment marked the sites of the old vesiculations, and these areas became raised and extended peripherally.

Examination reveals a darkly discolored hyperkeratotic lesion, 3 cm in diameter, with a surface of sandpaper texture on the lateral portion of the left leg. Radiating from this area there are numerous polyangular papules of similar character which vary in size from 2 mm to 2 cm in their greatest diameter. On the lateral surface of the right leg there is a similar confluence of polyangular lesions forming an area approximately 7.5 by 10 cm. Many of these papules are covered with a fine pale scale, while others show atrophic scarring. He also presents an enormous soft doughy tumor of the anterior left portion of the neck, which is approximately 10 cm in diameter and comprises a spongy mass of blood vessels covered by relatively normal skin.

Biopsy was as subsequently reported consistent with hypertrophic lichen planus.

#### DISCUSSION

DR B APPEL, Lynn, Mass. I am sure that no one can assume that the men who carefully studied the nomenclature for the "Standard Nomenclature of Disease" could have forgotten "lichen planus hypertrophicus." I looked it up and found "lichen sclerosus et atrophicus" and "lichen planus," but no other form of lichen planus is mentioned. I found nowhere a mention of the hypertrophic form of lichen planus, which, to my way of thinking, is a disease entity which merits inclusion in the "Standard Nomenclature of Disease." I presented this case because it happens to be the first case of hypertrophic lichen planus in a Negro that I have seen. At the Boston City Hospital a goodly number of Negro patients are seen. Imagine my surprise when I find another patient here today, a Negro woman, with lichen planus hypertrophicus. The incidence in Negroes probably is not so rare,

or this may be an extraordinarily rare coincidence. Apropos of the tumor on the left side of the neck, the patient stated that it came on after an injury ten years ago. It is my impression that he has a congenital hemangioma in that location which was latent and was stirred up by the injury. Typical of his race, he is solicitous and fearful that some doctor would want to cut it out. I promised him that no one here today would do that to him.

DR A. HOLLANDER, Springfield, Mass. I propose the name "lichen planus verrucosus" instead of "hypertrophicus" because it is the most commonly used term in the international classification and it also describes best the clinical picture of the lesion.

DR B. APPEL, Lynn, Mass. I should like to state that Dr. Hollander's remarks do not apply to the authoritative work to which I refer, which is the "Standard Nomenclature of Disease and Standard Nomenclature of Operations," published by the American Medical Association, which we, as dermatologists in this country, should feel compelled to follow. Dr. Hollander refers to the generally accepted term, lichen verrucosus.

DR J. H. BLAISDELL, Boston. I was going to comment on the term "lichen planus verrucosus" and whether its use clouds or clarifies the issue. This rare type of lesion is acuminate or conical, with central horny projection, which when coalescent forms rough, horny brownish patches, an irregular surface which has nothing to do with the name. The lesion in this case is hypertrophic. To exclude the term "lichen planus hypertrophicus" is not to clarify or improve the nomenclature.

#### CHICAGO DERMATOLOGICAL SOCIETY

LESTER M. WIEDER, M.D., *President*

MARCUS R. CARO, *Secretary*

Oct 18, 1944

**Dermatomyositis** Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS and DR. M. S. KAGEN

H. M., a Negro schoolgirl aged 17, was admitted to the Cook County Hospital on July 15, 1944, presenting scleroderma of the face, with contractures of muscles of the extremities and weakness of the neck and shoulder girdle, with limited movement of the involved areas and pain in the lumbar area and muscles of the neck. The symptoms appeared six months previously, following what was thought to be a simple sore throat of a few days' duration.

The skin of the face is bound down, making her appear expressionless. The rest of the skin is normal except for a depigmentation of the neck. The muscular involvement includes the neck, chest and the extremities, of which the proximal areas seem to be more affected than the distal. There are contractures about the joints of the shoulders, elbows, wrists, ankles and fingers. The left wrist is fixed, the fingers are in a state of flexion and seem to be fixed in that position, and the arms cannot be raised except for a short distance.

The patient has received sulfonamide therapy, without any appreciable improvement, and also various vitamins. Because of the inability to obtain penicillin, she was given neostigmine, with perhaps some improvement.

Examination of the blood revealed 3,950,000 erythrocytes and 9,900 leukocytes. The Kahn reaction was negative. The urine was normal. The electrocardiogram showed myocardial damage. The roentgenographic examination of the heart showed the cardiothoracic ratio increased.

The histologic examination of a section removed from the skin showed edema throughout the cutis with some compression of the epidermis. The blood vessels

were somewhat edematous, dilated and engorged. The cuticular appendages were not involved. The section removed from a muscle showed a vacuolar degeneration of the muscle bundles. There was an invasion of the bundles by an infiltrate of lymphocytes, with a perivascular infiltrate of lymphocytes, plasma cells, histiocytes and fibrocytes in some areas.

**Dermatomyositis** Presented by DR DAVID V OMENS and (by invitation)  
DR HAROLD D OMENS

H K, a schoolboy aged 13, was admitted to the Children's Hospital (Cook County Hospital) on July 2, 1943, because of an eruption accompanied with extreme weakness.

On examination there was a puffiness of the face, neck, body and extremities, on which was superimposed a patchy erythema. This swelling started on the face on April 7 and spread to the other areas in this order: face, neck, arms, abdomen and, lastly, legs. It was accompanied with weakness which involved the muscles of the neck and the proximal muscles of the extremities. The symptoms continued until the middle of June and gradually subsided. On about July 1, the weakness reappeared and became progressive to the point that the boy was unable to raise his head from the pillow.

On examination of the heart there is a blowing systolic murmur over the apex and pulmonic areas. The roentgenographic examination showed enlargement of the heart.

Examination of the blood revealed 3,840,000 erythrocytes and 13,800 leukocytes. The Kahn reaction was negative. The urinary creatinine was 590 mg per hundred cubic centimeters for twenty-four hours. The blood was sterile on culture.

This boy had received sulfonamide therapy without any appreciable results. He was then given penicillin, receiving a total of 1,200,000 units, 200,000 units the first day by the intravenous method and thereafter 5,000 units every four hours by intramuscular injections. Today the boy is able to get about with the aid of some support. The exanthem has faded somewhat, but the edema is still present.

Histologic examination of a section removed from the skin revealed relative hyperkeratosis of the stratum corneum and acanthosis of the prickle cell layer, which for the most part was intracellular but was also intercellular. The papillae and the subpapillary layer of the cutis were edematous, with dilatation of the blood vessels. The edema seemed to involve the entire cutis with engorgement of the deep blood vessels plus a cellular infiltration of the blood vessels, sweat glands and hair follicles.

The section from the muscle revealed parenchymatous changes in the muscle bundles, with vacuolar and hyaline changes. There was a diminution in the cross striations, with invasion of the muscles by an infiltrate composed of lymphocytes, plasma cells, histiocytes and fibrocytes which was greater about the blood vessels, with an engorgement of the vessels.

DISCUSSION OF THE CASES OF DERMATOMYOSITIS

DR JOHN F MADDEN, St Paul. I have a patient with early dermatomyositis in my service in the Ancker Hospital. The patient had extreme laryngeal and pharyngeal edema and dermatomyositis of the extremities. The eyelids and the V of the neck were heliotrope colored and edematous. This was the first case of early dermatomyositis I have seen treated with penicillin. He was given 100,000 units daily. An improvement in his voice and physical status was seen at the end of the third day. There was a decrease in the laryngeal edema. At the end of a week and a half the cutaneous changes were almost gone. At the end of three weeks there was no edema and the changes in the eyelids had entirely disappeared.

The penicillin was given intramuscularly, subcutaneously and intravenously. It was noted that the symptoms would become aggravated whenever the drug was administered intramuscularly, while if it was given subcutaneously or, particularly, intravenously more improvement was observed. He has now had penicillin for a period of six weeks, and he is ambulant.

DR S. ROTHMAN (by invitation) I should like to raise the question as to whether dermatomyositis can be regarded as a disease entity, particularly in its differentiation from diffuse scleroderma and from acute lupus erythematosus. It seems to me that in both these systemic diseases it is a matter of chance whether or not the striated muscles become involved and show the histologic picture of myositis. The muscular pain in addition to articular pain is a rather common clinical symptom in acute lupus erythematosus. Involvement of the muscles in the diffuse sclerodermatic process is even more common. I feel that the girl shown today has all the characteristic features of diffuse scleroderma and her case should be diagnosed as such.

DR DAVID V. OMENS One case presented a histologic picture of scleredema and the other a picture of scleroderma. The Negro girl showed scleroderma, while the boy showed scleredema. Whether there is a definite clinical entity of dermatomyositis I do not know. I do not believe that there have been enough cases studied or recorded to justify one in classifying it as a definite clinical entity. The conditions being as we see them, we must take it for granted that it is dermatomyositis. If not, what is it?

**Urticaria Pigmentosa** Presented by DR DAVID V. OMENS and (by invitation) DR HAROLD D. OMENS

S. B., a Jewish housewife aged 47, for the past eighteen years has had a dense, profuse maculation of the skin of the body and extremities. These macules are variable in size, from that of a pea to that of a bean, and reddish brown. They are devoid of subjective sensations, but on slight irritation they assume urticarial characteristics for a short period, after which they again become as they were originally. The maculation appeared after a surgical operation, while the patient was still in the hospital. At various times a diagnosis of secondary syphilis has been made.

The urine and blood were normal. The blood chemistry showed sugar 90 mg, urea nitrogen 15 mg, nonprotein nitrogen 31 mg, uric acid 23 mg, cholesterol 220 mg and creatinine 1.9 mg per hundred cubic centimeters.

The histologic examination showed some atrophy of the epidermis with intercellular and intracellular edema of the prickle cells, increased pigment in the basal layer and effacement of the papillae. There was edema throughout the cutis, with spacing between the collagen fibers. The blood and lymph vessels were dilated with mild perivascular cellular infiltration composed of mast cells.

#### DISCUSSION

There was no discussion of this case.

**Lichen Planus** Presented by DR DAVID V. OMENS and (by invitation) DR HAROLD D. OMENS

E. H., a Jewish housewife aged 53, presents a generalized eruption of six weeks' duration which is devoid of subjective sensation. The eruption involves the face, body and extremities, being most severe on the face as a diffuse eruption of small nodules, varying in size from that of a pinhead to that of a pea, of a shiny violaceous color, with scaling of the surface. While the eruption is diffuse on the face, it is discrete on the other areas.

The patient is shown today because she is from out of town and came in today unexpectedly for treatment.



The epidermis was only secondarily involved from the pressure beneath showing a thinning of the epidermis with almost complete effacement of the rete pegs, the corium presented superficial circumscribed nodules composed of epithelioid cells and almost complete absence of lymphocytes. The nodules seemed to be separated from each other by connective tissue septums, and there was an occasional ill defined giant cell. The infiltrate seemed to be in association with the blood vessels.

## DISCUSSION

DR CLARK W FINNERUD I understand that there were no histologic sections presented today. Because of several features, the distribution of the lesions, involving particularly the extensor surfaces of the face, with no lesions in the mouth, and the absence of itching, I think it will prove to be something other than lichen planus, possibly lymphoblastoma, in spite of the lichen-planus-like appearance of the individual papules. The sections should be presented at the next meeting whether the patient is presented or not. It is a very unusual case.

DR MAURICE OPPENHEIM (by invitation) I agree with Dr Finnerud that the clinical symptoms are not those of lichen planus. The color, the round shape, the absence of glossiness of the surface, the absence of itching and the lack of a central depression do not fit in with the diagnosis of lichen planus. I should like to exclude also the diagnosis of lupus erythematosus disseminatus, which shows scales, enlargement of the openings of the sebaceous glands and scar formation. It looks to me more like a case of disseminated papular sarcoid.

DR M R CARO A number of years ago I presented a patient with lesions that I thought were lichen planus with an extensive distribution on the extremities as well as on the face. There was a good deal of discussion as to whether the histologic picture was lichen planus or lupus erythematosus. At that time Dr Finnerud said that when on examination one cannot differentiate between lichen planus and lupus erythematosus the disease generally terminates eventually as lupus erythematosus. That of my patient did. I believe that in the case presented today one is dealing with atypical lupus erythematosus rather than lichen planus.

DR S J ZAKON The patient told me that the first time the eruption appeared she was receiving treatment for arthritis, probably with a gold preparation. There is a possibility of its being a gold dermatitis.

DR DAVID V OMENS I have had the patient under observation for about one month. At the time she first presented herself the papules were about the same as they are now, but they were more violaceous and there were no scales, hence we diagnosed the eruption as lichen planus. She has improved with colloid mercury therapy, this being the third treatment. She has had a gold preparation for arthritis and mercuric salicylarsonate for the eruption, given by her family physician.

**Pityriasis Lichenoides et Varioliformis Acuta (Habermann)** Presented by DR HERBERT RATTNER and (by invitation) DR H H RODIN

Mrs K K, a white woman aged 24, of Irish-American descent, complains of a moderately pruritic generalized eruption of five weeks' duration. She states that the eruption began suddenly on the back and has spread to involve all areas except the face. There are no constitutional symptoms. Her past history reveals nothing significant except for a mastoidectomy in 1933.

On examination there is a generalized eruption consisting of discrete vesicles, crusted lesions, superficial ulcers and lichenoid papules. The trunk is involved principally.

## DISCUSSION

DR MAURICE OPPENHEIM (by invitation) There is a superficial form of pityriasis lichenoides varicelliformis and a deeper form, which Mucha called

"varioliiformis" He was the first to present such a case Then I presented a second case, of more superficial type Habermann published a survey about his own and other cases The cause is not known The cases are always confusing grossly, and the diagnosis of pustular syphilis is always made The histologic examination shows chronic pityriasis lichenoides with a central superficial necrosis like that in true pityriasis varioliiformis

DR EDWARD A OLIVER I agree with the diagnosis I do not know whether dermatologists are learning to recognize the disease or whether it is commoner now, but I have seen 3 cases in the last year I saw 1 case several weeks ago through the kindness of Dr Omens

**Atrophoderma Vermiculatum (?)** Presented by DR EDWARD A OLIVER and (by invitation) DR SAMUEL M BLUEFARB

C P, a Negro woman aged 24, states that she first noticed "blackheads" on her face at the age of 16 They appeared first on the chin and then on the cheeks, chest, flexure folds and thighs The lesions commenced with "blackheads" which on extrusion left "holes" in the skin At present there are no signs of inflammation There is a permanent scarring with a few comedos still present In the pitted atrophic areas there is very little reticulation

The physical examination discloses no abnormalities except dental caries The blood pressure is 140 systolic and 90 diastolic

The hemogram showed hemoglobin content 11.5 Gm, erythrocytes, 4,560,000, and leukocytes, 5,000, with 70 per cent polymorphonuclear neutrophils, 24 per cent lymphocytes, 1 per cent eosinophils and 5 per cent monocytes The Wassermann reaction was negative The urine gave a 1 plus reaction for albumin

#### DISCUSSION

DR L H WINER, Minneapolis, Minn Through the kindness of Dr Michelson, I reported the case of a patient in whom this eruption was essentially an atrophy under the title of "Atrophoderma Reticulatum" (ARCH DERMAT & SYPH 34 980-988 [Dec] 1936) The comedos were not in the foreground In the histologic sections the para-follicular connective tissue had undergone atrophy and the elastic tissue in these regions had disappeared The follicles, sebaceous glands and hair follicles had become obliterated We called it atrophoderma reticulatum because it was reticulated-appearing atrophy

In the patient today the history is more or less that of acne In the foreground are the comedos Histologically, I could not see the atrophic changes I think that it is possibly a scarring with acne indurata

DR LOUIS A BRUNSTING, Rochester, Minn The reticulated scarring of the cheeks appears to be the end result of acne vulgaris There are clusters of comedos located elsewhere on the trunk and extremities, indicating that part of the same process is still active, a general stimulation of the pilosebaceous mechanism

DR EDWARD A OLIVER We thought that the scarring, especially on the chin, was a little extraordinary It was a necrotic, irregular type of scarring We showed the patient with the diagnosis of atrophoderma vermiculatum to promote discussion of eruptions that produce unusual scarring

**A Case for Diagnosis (Lichen Amyloidosis [?] in Two Sisters)** Presented by DR S W BECKER

Mrs T F, a white housewife aged 31, first noted itching of the legs associated with roughness and brownish spots in 1937 when she was four months pregnant The chief complaint has been constant itching Her health has been excellent Her father died at 46 with heart disease He is said to have had a dry skin but no lesions similar to those of the patients One brother, aged 33, and one sister, aged 23, have no such trouble One of the father's nieces had a red, dry skin

Small papules have been present on the arms and forearms for two years. On the legs were keratotic rough papules, which seemed to be confluent in some areas. On the thighs was a punctate brownish discoloration with the brown macules and papules in linear formation in places. Lichenoid flesh-colored papules were present on arms and forearms.

One sister, Mrs. E. H., a housewife aged 29, has had a similar eruption on the legs and thighs since about the age of 8. For five years she has had small papules on the arms and forearms. The thighs and especially the legs showed keratotic rough papules, brownish in color. Small lichenoid flesh-colored papules were seen on the arms and forearms. The eruption is pruritic, especially in hot weather.

The histologic examination of specimens from both patients showed hyperkeratosis, elongation of the rete pegs, melanotic hyperpigmentation and widening of the papillae, in many of which were masses of homogeneous material giving a faint reaction by stains for amyloid.

#### DISCUSSION

DR. RUBEN NOMLAND, Iowa City. I think these sisters present an unusual picture of localized amyloidosis. It must be unique to occur in a family group. The lesions on the legs are like those of lichen amyloidosis, those on the arms are lichenoid. The papule stains were not too satisfactory. I believe further substantiation that this is lichenoid amyloidosis is necessary. I suggest that a congo red test be done. That will show positive if it is amyloid and negative if it is not. (Nomland, R. Localized [Lichen] Amyloidosis of the Skin, *ARCH. DERMAT. & SYPH.*, **33**: 85 [Jan.] 1936).

ADDITIONAL NOTE.—Dr. Becker sent me sections to be stained. When these were stained in very dilute gentian violet and mounted in glycerin the amorphous material in the papillary layer took up a distinct red color typical of localized amyloid of the skin.

DR. H. E. MICHELSON, Minneapolis. In the diagnosis of amyloidosis of the skin one has three methods: first, the clinical, which is not too certain, second, the histologic, and, lastly, the congo red test. In the cases presented I saw nothing that was positive enough to allow me to accept the diagnosis of amyloidosis. The only other thought I had was that the disease might be follicular ichthyosis. They mentioned that the father had something similar.

DR. S. W. BECKER. When I saw these patients I thought the eruption was an exaggerated type of follicular hyperkeratosis. However, the hyperpigmentation on the thigh of the first patient is unusual for that disease. I took a biopsy specimen from the leg and thigh of both patients. We noticed that the dilated papillae contained material which stained red with hemalum, erythrosin and saffron stain. With special stains for colloid, amyloid and other chemical substances, the only positive result was the rather faint stain by the methyl violet and the congo red method. They were, therefore, presented with a tentative diagnosis of lichen amyloidosis. The severe degree of the itching is unusual for follicular hyperkeratosis.

**Alopecia Areata in Twins.** Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS.

Twin brothers, aged 20, present a patchy loss of hair of the scalp and eyebrows.

#### DISCUSSION

DR. JAMES H. MITCHELL. Some years ago I had the opportunity of seeing twin sisters with alopecia areata. The first one examined had an extensive loss of hair. Treatment with a quartz lamp had no effect, but the alopecia promptly cleared with trichresol. When the sister came in, I tried trichresol, with no effect, then I changed to use of a quartz lamp, and she improved.

**Acanthosis Nigricans (Juvenile Type)** Presented by DR DAVID V OMENS and (by invitation) DR HAROLD D OMENS

Y B, a Jewish schoolboy aged 18, is being treated for dermatitis herpetiformis and presents additional features involving neck, chest, axillae, umbilicus and groins in the form of deep pigmentation with a verrucous-like thickening of the skin. There are no subjective sensations associated with the pigmentation, in fact, he was not aware of it until it was called to his attention. This boy weighs 250 pounds (113.4 Kg) and has gained 50 pounds (22.7 Kg) in the last four years.

All the laboratory tests, including a determination of the basal metabolic rate gave normal results. One older brother weighs as much as the patient but has no involvement of the skin.

The histologic examination of a specimen removed showed relative hyperkeratosis, with acanthosis of the prickle cell layer with intracellular edema of the prickle cells, increased pigment of the basal and dendritic cells, with few chromatophores with pigment in the upper portion of the cutis, and considerable papillomatosis with edema of the connective tissue, dilatation of the blood vessels and a lymphocytic perivascular cellular infiltration in the upper portion of the cutis.

## DISCUSSION

DR THEODORE CORNBLEET I think that the patient presents evidence of the juvenile form of acanthosis nigricans. There are additional changes which suggest the possibility of Cushing's syndrome. Of course, the latter has changes in the pituitary, but the adrenal glands, too, may be involved. These adrenal changes and perhaps affection of the chromaffin system could be the common denominator for acanthosis nigricans and Cushing's syndrome. They appear to overlap in places. It would be fortunate if some one could perform an exploratory operation on the abdomen just at the time when the earliest recognizable changes were occurring in acanthosis nigricans. As yet their exact site is not known.

DR S ROTHMAN (by invitation) The tendency to formation of striae in the juvenile type of acanthosis nigricans has been noted in several cases, and this feature, together with the buffalo type obesity and renal glycosuria, makes one believe that possibly there is some relation between Cushing's syndrome and the juvenile type of acanthosis nigricans. It would be interesting to know the values for blood pressure when the patient is at rest and the values following exertion in the case presented.

DR HERBERT RATTNER The juvenile type of acanthosis nigricans is usually considered to be benign and unassociated with a malignant tumor elsewhere. An article recently published by Helen Curth, however, points out that the juvenile type is in fact not infrequently associated with visceral malignant growths. If I recall correctly, her conclusion was based on the results of some cases studied by her and a review of the literature.

**Lymphoblastoma** Presented by DR THEODORE CORNBLEET and (by invitation) DR D M COHEN and DR H C SCHORR

R G, a white man aged 72, has several lesions on the chest and a single large one on the extreme upper portion of the back. The lesion on the back has been present for five months, and is a smooth tumor mass, the size of a small orange, not very well defined, with a purplish hue and movable with the skin. The mass is not painful but is somewhat tender. There are infiltrations of a patchy character over the upper part of the chest and shoulders. The superficial lymph nodes are enlarged and movable. The spleen is not palpable nor is the liver, but the latter is slightly tender.

The Kahn reaction of the blood serum was positive, but the Wassermann reaction was negative. Examination of the blood showed 84 per cent hemoglobin and 6,350 leukocytes, with 74 per cent polymorphonuclears, 3 per cent eosinophils, 14 per cent lymphocytes and 9 per cent monocytes.

The smears from the bone marrow obtained by sternal puncture were obtained by Dr S O Schwartz the hematologist at the Cook County Hospital, who reported that the marrow was essentially normal as far as cells were concerned. The megakaryocytes were present and appeared normal. The nucleated erythrocyte to leukocyte ratio was approximately 1:2. The erythroid maturation was normoblastic, and granulocyte maturation was also normal. There was apparently some increase in the blast cells which in view of the clinical observations probably belonged to the lymphoid series. No subsequent increase in lymphocytes was seen. The diagnosis was probably early lymphoblastomatous invasion of the marrow.

The roentgenographic examination of the chest gave normal results.

The histologic examination of a specimen taken from the chest showed a flattened epidermis and the upper part of the corium free from pathologic changes. Deeper in the corium the sweat glands and some of the blood vessels were surrounded by densely packed mantles of a cellular infiltrate composed largely of lymphocytes. About a deeper nerve the infiltrate contained also many larger pale cells. Invading the hypoderm there was a circumscribed, large, densely packed cellular mass containing many lymphocytes and reticulum cells with a few mitotic figures present.

#### DISCUSSION

DR RUBEN NOMLAND, Iowa City. I thought it was not a lymphoblastoma, but was probably a metastatic neoplasm. I believe the cells were not those of lymphoblastoma but of a high grade neoplasm which may be epithelial in origin or possibly a sarcoma. I think it is a metastatic tumor from a neoplasm located elsewhere.

DR LOUIS H. WINER, Minneapolis. I was interested in the histologic sections. I agree with Dr. Nomland that a high degree of malignancy is indicated by the histologic appearance. The cells are all of the same size and shape, and the whole histologic picture is a monomorphous cell proliferation, a condition seen in terminal lymphoblastoma or reticulum cell sarcoma.

DR FRANCIS W. LAMB, St. Paul. The question of metastases versus local development of such lesions has been discussed in a recent article by Robb Smith, a pathologist, in the *British Journal of Dermatology*. His discussion of all the conditions that fall into this group was from the viewpoint of the pathologist rather than the dermatologist, but any one who has not yet read the article will probably gain from it.

DR M. R. CARO. I thought that histologically it was consistent with the diagnosis of reticulum cell sarcoma. In the large mass of infiltrate the cells were reticulum cells and there were a number of mitotic figures present.

DR THEODORE CORNBLUTH. This mass had a large number of enlarged lymphatic glands. I am sorry we did not take one out for sectioning, because it might have shown something significant. We thought that the most likely diagnosis was lymphosarcoma. This is not contradicted by the histologic changes in the cutaneous lesions.

#### A Case for Diagnosis (Syphilis?) Presented (by invitation) by DR S. ROTHMAN and DR A. L. SHAPIRO

R. M., a white man aged 46, noted a painless lesion at the base of the penis in January 1944, six to eight weeks after extramarital intercourse. Local treatment and roentgen ray therapy failed to heal the lesion. About two or three weeks later, he consulted a dermatologist, who, after dark field and serologic examinations, instituted intravenous and intramuscular antisyphilitic therapy and applied mercury ointment locally.

In June 1944, a pruritic, scaling, erythematous eruption appeared on the arms, thighs and chest. Antisyphilitic therapy was stopped, and for the next five weeks treatment was directed against the eruption. Then biweekly injections of mercury (?) into the hip were started, the last one being given on October 9.

Shortly after the dermatitis appeared, in June 1944, a hemorrhagic blister was noted in the right palm, the blister dried to a crust. The process spread and in a couple of weeks broke down, oozing serum. The lesion continued to grow in area and in depth and contained pus. Sulfathiazole orally and mercury ointment locally, as well as hot compresses of magnesium sulfate solution, did not prevent the spread of the lesion.

Toward the end of August a similar lesion appeared on the left shin which then developed as did the one on the right palm.

The patient was admitted to Albert Merritt Billings Hospital on Oct. 13, 1944. He presents on the distal portion of the right palm a tender, round, ulcerating and granulating lesion, 30 mm in diameter, which is oozing a seropurulent material and is surrounded by a bluish erythematous halo. The right hand is moderately swollen. A similar lesion, 25 by 30 mm in area, is present on the left shin, 12 cm from the patella. A dried, crusted lesion is evident over the patella.

Results of laboratory studies were as follows. The Wassermann reaction was strongly positive 3,3, the Kahn reaction, very strongly positive (4 plus), the results of urinalysis, normal, the leukocyte count, 8,700, with 84 per cent polymorphonuclear neutrophils, 1 per cent large lymphocytes, 9 per cent small lymphocytes and 2 per cent basophils, erythrocytes, 4,950,000, and hemoglobin content, 15.6 Gm.

The roentgenographic examinations made elsewhere on Oct. 9, 1944, revealed generalized decalcification around the interphalangeal joints of the right hand but no evidence of osteomyelitis. The roentgenogram of the chest reveals several calcified nodes and a small soft caseous lesion in the right subapical region.

The histologic examination of sections from both lesions showed granulation tissue with acute infection but no specific changes.

The bacteriologic examinations gave the following results. In droplets of pus spores could not be seen. In smears from the lesion on the palm stained with Giemsa stain plump bacilli in chains were present. On blood agar plates gram-negative rods and gram-negative diplococci grew. In the broth cultures gram-positive and gram-negative rods and a few staphylococci were found. From the lesion on the leg staphylococci and large gram-positive rods were cultured.

The patient has ichthyosis vulgaris.

#### DISCUSSION

DR. MAURICE OPPENHEIM (by invitation). This very interesting patient came to my office in June 1944, sent to me by Dr. Sandoz, of South Bend, Ind. He was treated with roentgen rays and came in with a deep ulceration in the penoscrotal region. The patient told me that his serologic reactions were negative. I made the diagnosis of an ulcerated gumma and admitted him to a hospital. There the reactions were positive, though there was no history of syphilis. He responded well to treatment. He was at first given iodine and mild mercurial ointment U. S. P., later he was given arsphenamine and bismuth, and at home the injections of neoarsphenamine and bismuth were continued.

He returned to me with a neoarsphenamine dermatitis. I stopped treatment and gave him sodium thiosulfate. The gumma was healed completely. After four weeks he came back with a lesion on the right palm. I first thought of a secondary infection with *Staphylococcus* because he had often had such infections. I sent him back to Dr. Sandoz, who treated him with sulfathiazole. Then he came back, and because the lesion on the palm had grown larger I made a biopsy. I was suspicious that it might be a malignant tumor. It was not. I found histologic changes indicating syphilis. I sent him back to Dr. Sandoz and told him to try a mild antisyphilitic treatment with iodine and mild mercurial ointment. Then the patient disappeared from my care.

I believe that this is some kind of syphilis ulcerosa in a patient who is a heavy drinker. He drinks one or two bottles of heavy wine daily and therefore he has recurrences of his syphilis. The histologic observations confirmed this diagnosis.

I believe he should be treated with Zittmann's decoction, which was used in Vienna very often in cases of malignant syphilis, of syphilis which did not yield to any treatment and of syphilis which was overtreated. Zittmann's decoction contains guaiac, sarsaparilla, sassafras, and other wood decoctions, sometimes with a trace of mild mercurous chloride or iodine. I had the best experiences in such cases and I would ask Dr Rothman to try this treatment in this case.

DR LOUIS A. BRUNSTING, Rochester, Minn., Is the patient taking bromide?

DR S. ROTHMAN: No.

DR M. R. CARO: Has he had fever therapy?

DR S. ROTHMAN: No.

DR M. H. EBERT: I am inclined to think that this should be classified as malignant syphilis. This is the type that does not respond to ordinary therapy. These are premature gummas, as Dr Winer suggests, and I agree with him that this is a case in which it would be excellent to try penicillin.

DR S. ROTHMAN (by invitation): According to the history, the lesions developed while the patient was under antisyphilitic therapy. Thus, if the lesions are gummas this patient's case represents therapy-resistant syphilis. I should not like to go back to the old-fashioned sarsaparilla treatment, because it causes extremely unpleasant diarrhea. To change the reactivity in therapy-resistant syphilis, fever treatment has proved to be the method of choice. In the department of Dr S. W. Becker excellent results were obtained when fever was followed by injections of arsphenamine and mercurial rubs. This patient had an arsenical dermatitis, and therefore we cannot treat him this way. We intend to treat him with penicillin. The disadvantage will be that cure by penicillin will not decide the main differential diagnostic problem, namely, whether these lesions are gummas or deep pyogenic lesions in a man with decreased resistance to infection.

NOTE (Nov. 12, 1944).—The patient has had rapid clearing under penicillin treatment. His serologic reactions are still strongly positive.

#### A Case for Diagnosis (Bullous Eruption) Presented by DR THEODORE CORNBLFET and DR HERBERT RATTNER

T. P. K., a Japanese man aged 52, a physical culturist, has shown cutaneous changes for three years. Seven years ago he had an attack of poison ivy dermatitis in the summertime, for which he received ultraviolet rays. During several subsequent summers he had an eruption about the neck. These lesions would last two weeks. Three years ago the eruption involved all parts of the head as well as the neck. A physician prescribed sulfathiazole, after which vesicles appeared in the cubital fossae. Another drug was substituted for the sulfathiazole, but blisters began to appear and remained for four months. He was then hospitalized for three months, with no relief. The eruptions at that time were on the shoulders and hips and at the elbows and knees. Since then he has had some bullae appearing at short intervals, which are always preceded by pruritus.

The patient is better than he was two and one-half years ago in the sense that he does not have as many blisters and they do not occur as frequently. He does not think that trauma plays much of a role in the production of these lesions. On the other hand, he feels certain that the eating of eggs can produce them. At the present time, he shows a number of bullae in various stages of evolution and atrophy at the site where the greatest number of lesions appear. These tend to be grouped about the extremities and joints especially. There are some vesicles present in the mouth. The Nikolsky sign is present.

The patient has received acetarsone, vitamin A and applications of boric acid ointment.

The urinalysis showed albumin (2 plus). Examination of the blood showed 67 per cent hemoglobin, 76 per cent polymorphonuclears, 1 per cent eosinophils, 18 per cent lymphocytes and 4 per cent monocytes. The Kahn reaction was negative.

## DISCUSSION

DR H E MICHEISON, Minneapolis What therapy was used?

DR F E SENEAR He was in our hospital for a time Dr Stubenrauch saw him He had a generalized bullous eruption with erosions in the mouth I do not remember the therapy that was used As I remember, the eruption had nearly cleared up, but within a month after he left the hospital he had a recurrence

DR THEODORE CORNBLEET Of the bullous eruptions, we thought of pemphigus and dermatitis herpetiformis The lesions are more generalized today than they have been Prior to this the cutaneous changes have been almost entirely confined to the hands and feet and the joints Some of them follow trauma That made us think, therefore, of epidermolysis bullosa of the dystrophic variety The histologic changes are in keeping with such a diagnosis There was improvement with acetarsone, but there is a relapse today The patient needs further observation to come to a more definite conclusion about his disease

**Congenital Cutaneous Atrophy on Hands and Shins, Recent Dysphagia**

Presented by DR JAMES H MITCHELL

The patient, a man aged 52, stated that when he was a child bullae developed on all areas of his skin after slight trauma The palmar surfaces have since become resistant to trauma, allowing him to play baseball and to do the hardest kind of manual labor The lesions on the skin, however, remain tender and are easily traumatized The lesions appeared about two weeks after birth The feet have been free at all times No other member of the family is so affected

## DISCUSSION

DR M R CARO When I first looked at the patient, my impression was that this was a case of epidermolysis bullosa with no bullae at present When I questioned him he said that the lesions started as blisters The history that he is able to do hard manual work without producing lesions, however, is somewhat inconsistent with that diagnosis

DR STEPHAN EPSTEIN, Marshfield, Wis The patient states that his blisters follow trauma I believe that the clinical picture, the history and the stricture of the esophagus, which he has, would fit in with a diagnosis of epidermolysis bullosa

**Juvenile Xanthoma (Nevoxanthoendothelioma of McDonagh)** Presented (by invitation) by DR S ROTHMAN and DR Z FELSHER

D L, a 5 month old full term baby, normal at birth, suddenly began to have a generalized eruption, including the scalp, at 2 months of age The lesions have persisted, and new ones continue to appear No apparent sensation has been noted accompanying the eruption

The physical examination shows a generalized eruption consisting of yellow to yellowish red papules, the largest being about 6 mm in diameter The mucous membranes and deeper structures are not involved

The laboratory examination revealed a leukocyte count of 12,100, a hemoglobin content of 11.5 Gm and a normal differential count The tuberculin test (1:1,000) elicited a negative reaction The roentgenographic findings of the skull and chest were normal The total lipids in the serum were 635 mg per hundred cubic centimeters, and the cholesterol 195 mg

The histologic examination showed the epidermis atrophic The corium was filled with masses of closely packed large cells with finely granular cytoplasm and large well stained nuclei The sudan IV stain showed extensive deposits of lipid material throughout the corium

This case is similar to those discussed in the paper of Senear and Caro (*ARCH DERMAT & SYPH* 34 195 [Aug] 1936) In another case under our observation,



the eruption disappeared spontaneously after two years' duration. The picture of that patient is presented.

## DISCUSSION

DR M R CARO. This case is similar to the one reported by Dr Senear and me. The only histologic difference between the lesions in this case and those in ours was the absence of Touton giant cells in the present case. I do not believe that this is important, because they might be found if another part of the specimen were examined. I agree with the diagnosis as presented.

DR S ROTHMAN (by invitation). This disease was so well described by Drs Senear and Caro in 1936 that I have nothing to add. In our earlier case, the picture of which has been presented, all lesions disappeared spontaneously and did not recur during a period of two years.

**Linear Scleroderma** Presented (by invitation) by DR S ROTHMAN and DR A L SHAPIRO

W G, a 5 year old boy, was first examined in the dermatologic clinic of the University of Chicago on Oct 9, 1944. He presented flesh-colored to waxy edematous and indurated lesions varying in size from that of a split pea to that of a large plaque, on the shoulders, arms and thighs, distributed segmentally along the course of the fifth and sixth cervical and first and second lumbar nerves. Within the indurated areas slightly atrophic spots could be discerned. Contracture of soft tissues prevents complete extension of the right elbow.

The mother stated that the cutaneous lesions were first noted when the patient was 6 months old. At 9 months of age, he had severe bronchitis and convulsions. He has otherwise been normal. He has two siblings, who are healthy. There is no pertinent family history.

The erythrocyte count was 4,040,000, leukocyte count 5,000 and hemoglobin content 13 Gm. The urinary values were normal. Fluoroscopic examination of the chest revealed nothing abnormal.

The histologic examination showed a slight degree of homogenization of the collagen in the upper part of the corium.

## DISCUSSION

DR S W BLACKER. This boy presents a striking picture. It is certainly not linear scleroderma as it is usually seen. Persons with the latter usually have one or perhaps two definitely circumscribed lesions, usually along the extremities. This boy has a limitation of motion in the right elbow. I am not sure whether it is due to contraction of fibrous tissue, to a bony change or to some fibrosis in the joint. I believe that this child presents a disorder of fibrous tissue, but just how it should be classified I do not know.

DR LOUIE H WINER, Minneapolis. Histologically, the connective tissue showed intense edema, something that one does not see in scleroderma. In scleroderma there is an increase in the number and size of the cells. I could not make a diagnosis histologically. Clinically, I think that the disease is scleroderma.

DR S ROTHMAN (by invitation). I think that this is typical *scleroderme en bandes*, which in practically all cases follows segmentary distribution. I do not know of any other disease with induration, fibrosis, atrophy of the surface and segmentary distribution. The edema in the histologic picture is compatible with this diagnosis, because the disease shows three not sharply separated developmental phases, i. e., edematous, indurative and atrophic.

**Pigmentary Disturbance of the Skin (Poikiloderma of Civatte, Berlocque Dermatitis?)** Presented by DR I M FEISHER (by invitation) and DR E P LIEBERTHAL

B E, a Mexican woman aged 57, was admitted to the dermatologic department of the Mandel Clinic (Michael Reese Hospital) on June 20, 1944. At that time

she presented a mottled grayish brown pigmentation of the forehead, cheeks, chin and neck which had been present since 1941. The pigmentation was heaviest over the forehead and chin and in the areas anterior to the ears. Over the neck, nose, upper lip and center of the cheeks, the grayish brown discoloration was comparatively lighter and mixed with larger or smaller islands of normally colored skin. The patient complained of burning and itching sensations over the involved areas.

In 1941 the patient consulted a Mexican healer, who advised the rubbing of fresh roses sprayed with perfume over her face and neck for short periods each day for nine days to allay the symptoms of nervousness, headache and gastrointestinal disturbances. The pigmentation of the skin began shortly after that. No history of the use of silver salts or mercurials in cosmetics could be elicited. The patient has been using cold cream and face powder only casually. She has been in the climacterium since 1938. Diagnoses of chronic myocarditis, pathologic-functioning biliary tract, and frontal and ethmoidal sinusitis have been made in other departments. Results of the laboratory examinations, which consisted of complete blood counts, urinalysis, serologic tests, examinations of stools, determinations of the basal metabolic rate and blood chemistry examinations, were all within normal limits.

The histologic examination of a section removed from the forehead revealed a mild edema of the epidermis and an infiltrate of the papillary layer consisting of round cells, fibroblasts and histiocytic cells, many of them containing fine granules of melanin. The infiltrate is heaviest in the papillary layer, about the blood vessels, hair follicles, sebaceous glands and sweat glands.

#### DISCUSSION

DR F E SENEAR. I presented a woman a year or two ago with a picture very much like this and suggested two possible diagnoses, poikiloderma of Civatte and lupus erythematosus. The major opinion at the meeting was that the disease was probably lupus erythematosus, and subsequent microscopic studies showed that it was. This patient presented some very distinct depressions and some distinct follicular plugging in the temporal region. I feel that will prove to be lupus erythematosus rather than poikiloderma of Civatte.

DR S W BECKER. This disorder could be caused by several things. It is possible to obtain such a picture following photosensitization and after the application of oily and tarry substances, among which are perfumes. In the German "Handbuch" such melanotic disturbance has been mentioned as occurring after exposure to oil in industry. I recently saw a patient who had been working with oil, and he had a similar eruption. However, he had had intense anemia and pains in the joints which strongly suggested lupus erythematosus. I think that further observation is the only solution to the problem.

DR I M FELSHER (by invitation). We considered the diseases mentioned and also lupus erythematosus, but the histologic section did not bear out the diagnosis of lupus erythematosus and therefore it was not included in the presentation. We also thought of the possibility of some endocrine disturbance. It was the symptoms of the climacterium that caused her to seek relief, and the menopausal syndrome could be responsible for the pigmentation.

**Dermatitis Due to Nail Coating** Presented by DR L F WEBER and (by invitation) DR C H STUBENRAUCH JR

E A, a carpenter aged 61, first had an eruption on the left hand six weeks ago. After two weeks the right hand and forearms were involved.

On September 27, he had a bright and shiny redness on the webs and sides of the left fingers. The left palm was thickened and scaly. The forearms showed a diffuse, bright redness. A patch test on the left arm with nail coating showed redness at the end of twenty-four hours. When he stopped work and used bland applications the dermatitis disappeared. He returned to work on October 16, and

a flare-up of his dermatitis followed within twelve hours. His present attack shows redness and vesiculation of the previously involved sites.

## DISCUSSION

DR MAURICE DORNEL: I have been seeing a large number of eruptions of this type recently. The nails are covered with a gelatinous coating, which, as I have been informed, is applied to make them hold better and to prevent the wood from cracking. In all instances the eruption first appears on the left fingers and hand and then spreads to the left forearm and the right hand. I am now investigating this matter.

DR S. J. ZAKON: When industrial dermatologists see such dermatoses in workmen, dermatologists in general practice should think of such contacts in the consumer. I have seen a number of cases of dermatitis in men working with varnish.

DR H. E. MICHIGSON, Minneapolis: Those of us who are called on to settle occupational cases have a terrific responsibility, and I should like to hear how Dr. Weber handles such a case. The man being a carpenter, is he going to be allowed to go back to his occupation? One must constantly keep in mind that even though a certain substance is incriminated, occupations have many, many risks and the combination of circumstances may bring about the dermatitis.

DR L. F. WEBER: Dermatitis caused by the resin coating on wire nails was unfamiliar to me until several months ago. The manufacturer knew about it, according to his letter. Dermatologists had received no help from him until I asked for it. The manufacturer was kind enough to supply me with a list of the ingredients in the resin coating.

My first experience with the resin coating on the wire nails causing a dermatitis occurred about one year ago, but I did not know it until recently. My second experience was no different, until several patients with an unusual dermatitis and a suggestive history located the causal factor. From then on it was simple, as more patients continued to report with a dermatitis and a similar history.

The history was as follows: The webs and sides of the fingers were involved first, next the back of the left hand and the left wrist, later the right hand and the right palm. There was a distinctive color to the eruption, consisting of a glistening redness, which gave the surface a polished appearance. There could hardly be any mistake about the fact that the dermatitis originated in the occupation. The employees nailed boxes for foreign transportation. This brought them into contact with pine wood and wire nails. In my experience pine wood is seldom a cutaneous irritant.

Once the carpenters were removed from the occupation the dermatitis disappeared. On resuming work, they had a recurrence within a day or two. Patch tests were made with resin removed from the nails. Not all patch tests elicited positive reaction. The coated nail left in direct contact with the skin in 1 patient did not reproduce a dermatitis. It was my impression that sweating was an aggravating factor. The rough surface on the wire nail due to the deposit of resin makes the nail remain firmer in the wood.

The composition of the coating is as follows: 40 per cent by weight of selected resins and linseed oil, 35 per cent by weight of alcohol, 25 per cent by weight of petroleum distillates.

The coating is applied by the wire nail manufacturers in liquid form. It dries rapidly, and the only material that is left on the nails is the 40 per cent of selected resins and linseed oil.

I am unable to answer Dr. Michelson's questions. I know that the majority of patients are unable to handle the nails coated with resin. They must change jobs. If this means a loss of earning power, the occupational laws provide some compensation.

DR STEPHAN EPSTLIN, Marshfield Wis. I should like to confirm Dr Weber's observation that sensitivity to pine is very rare. There are a good many factories around Marshfield using white and yellow pine. When sensitivity occurs, it is usually due to some other factor and not to the pine.

**A Case for Diagnosis (Xeroderma Pigmentosum?)** Presented (by invitation) by DR M OPPENHEIM and DR D COHEN

J K, a retired mail clerk aged 73, presents an eruption involving the scalp, face, neck, trunk and upper extremities. In the foreground of this picture is the scarlike formation of the entire scalp with the exception of two clusters of hair in the parietal and occipital areas. The skin is white and shiny and is fixed to the bone. No movement of the skin is possible. There are many excoriations and depressed scars the size of peas. There are a few scaly flakelike areas. On the parietal and occipital areas there are many areas of brown pigmentation interrupted by white nonpigmented irregular areas.

The skin on the neck is thickened with parallel wrinkles in stripe form running from the occiput to the back. Behind the left ear, below the mastoid process, a superficial ulceration is present with irregular margins in an indurated area.

The face is stained brown and white, with telangiectasia on the nose and cheeks. The veins of the temporal areas are translucent. There are chronic conjunctivitis and madarosis.

The skin around the nose and upper lip is soft and can be folded. The areas in front of the ears are hard, the skin cannot be picked up between the fingers. The limits are sharp like a plate embedded in the skin. On the lower part of the chin many hyperpigmentations are present. Around the mouth there are radial wrinkles. The hair of the beard is normal. The lips are of a normal red color.

On the anterior part of the neck the skin has a normal elasticity. The white color is interrupted by many sharply limited hyperpigmentations like freckles. Over the sternum, the skin is indurated and difficult to fold, as in scleroderma. The surrounding skin over the breast, shoulders and arms has a partially pink and partially white color, normal consistency, many telangiectases, freckles and a few cavernomas.

On the dorsal aspect of the hands there are scarlike atrophic areas with transparent blood vessels. The peripheries of these areas are hyperpigmented, and the hairs are absent. The skin over the fingers reveals slight changes. The nails are split, fragile and deformed.

The eruption started on his hands, face and neck about eight years ago. It seemed to follow exposure to the sun, occurring mainly in the summer. The eruption consisted of blisters which were not attended with any pruritus. The blisters occurred for five or six years. During the last two years these blisters have gradually disappeared. He has a "nervous" habit which causes him to dig into his skin with his nails, resulting in some scarring.

The Kahn reaction was negative. The urine was normal. An examination of the blood revealed 4,870,000 erythrocytes, 15 Gm of hemoglobin and 11,100 leukocytes, with a differential distribution of 70 per cent segmented forms, 4 per cent eosinophils, 1 per cent basophils, 17 per cent lymphocytes and 8 per cent monocytes.

The histologic examination of a lesion removed from behind the left ear revealed a hyperkeratosis and acanthosis of the epidermis. The epithelial connective tissue border was sharp. There was a round cell infiltration in the subpapillary layer. The blood vessels of the subpapillary layer were enlarged and the deeper layers of the connective tissue hypertrophic with scant connective tissue cells. There were no signs of carcinoma.

#### DISCUSSION

DR HARRY R FOERSTER, Milwaukee. I thought that this case was suggestive of a factitious dermatitis. The uniformity of size of the apparently excoriated lesions and scars, their distribution over areas accessible to the finger nails and

the absence of eruption in other areas suggest that as a possible diagnosis. Although he gave a history of vesicular lesions as early manifestations of the eruption, he has had no vesicles recently. The lesions on the cheeks, however, do not fit in with this diagnosis and confuse the picture.

DR S. ROTHMAN (by invitation). I have been impressed by the fact that the patient displays two sharply limited strips free of pathologic changes, corresponding to the straps of his underwear. Also, the distribution as a whole strongly suggests that one is dealing here with a condition of sensitivity to ultraviolet radiation similar to xeroderma pigmentosum. There are a good many cases of xeroderma pigmentosum on record with late onset. I myself reported such a case in 1923 (*Arch f Dermat* **144**: 440). This patient shows spotted hyperpigmentation and depigmentation, atrophy, telangiectasias and keratoses, a picture which is similar to actinodermatitis, on the one hand, but almost identical with that of xeroderma pigmentosum on the other. The similarity of these two conditions was discussed in the paper just referred to.

DR STEPHAN EPHSTEIN, Marshfield, Wis. Dr Rothman believes that this is a case of photosensitivity. The same thought occurred to me, that this might be some form of xeroderma pigmentosum.

DR H. J. PARKHURST, Toledo, Ohio. I saw no keratoses in this patient, but it is true that involvement is limited to areas exposed to sunlight. I thought it might fit more into the classification of hydroa vacciniforme.

DR F. W. LYNCH, Minneapolis. I hesitate to accept the suggested diagnosis of xeroderma pigmentosum because of the late age of onset and because there are lesions on the upper portion of the chest in an area beyond that usually exposed to light. The sharp limitation of the eruption particularly to areas on the dorsa of the hands, the absence of keratoses and the fact that the nose, lower lip and ears present changes no severer than those in other areas are also against a diagnosis of xeroderma pigmentosum. I agree with the suggested diagnosis of iactitious dermatitis. I think, in addition, that one might consider some other previous follicular scarring process, even lupus erythematosus, though there is little at present to suggest that diagnosis.

DR S. ROTHMAN. To me the man admitted that in summer he crosses his back yard without a coat, clad only in his underwear.

DR MAURICE OPPLHEIM (by invitation). This man is sensitive to sunlight. The location is definitely on the exposed areas of the skin—hands, face, cheeks and neck. My first impression was that of roentgen ray dermatitis, because with that there is hypertrophy, atrophy and ulceration of the skin. I thought that the ulcer on the left side of the head might be an epithelioma and made a microscopic examination. The findings were absence of pigmentation, hypertrophy of the connective tissue, round cell and plasma cell infiltration and no cancer (the section was possibly too superficial). I thought of some kind of sensitivity to sunlight and then of other photosensitivity disease, like a kind of xeroderma pigmentosum. When the patient was a boy he was sensitive to sunlight. Later he was a railway mail worker and was exposed to the sun. He contracted erythema several times, then he avoided the sun entirely. There is no hyperkeratosis. Telangiectasia and hyperpigmentation are present but not the follicular hyperkeratosis that is sometimes seen in these chronic cutaneous changes caused by light.

I do not believe that this is a real xeroderma pigmentosum of Kaposi, as Dr Rothman thinks it is, because it is caused by a congenital hypersensitivity to sunlight, but I think that the actinic rays of the sun are the cause of this disease. An examination for porphyrin could not be made.

#### A Case for Diagnosis (Pemphigus Erythematosus Limited to the Nose?)

Presented by DR CLARK W. FINNERUD

J. H. K., aged 31, was first seen six months ago because of an eruption of the distal half of the nose of about two years' duration, which followed sunburn. The

eruption was not accompanied with subjective symptoms. None of the lesions had disappeared, nor had they improved from various forms of treatment. There had been no lesions elsewhere at any time. The treatment has included roentgen therapy, local preparations, nonspecific protein therapy in the form of injections of typhoid vaccine, a series of injections of gold sodium thiosulfate and injections of nicotinamide. No biopsy has been performed.

The examination reveals a rather sharply demarcated, erythematous, scaling and crusting plaque on each ala nasi and on the tip of the nose.

#### DISCUSSION

DR F E SENEAR. I think that this is a very interesting case. A localized eruption of that sort of course makes one think of lupus erythematosus, but I was unable to make out any clinical characteristics that would support that diagnosis. The other alternative is pemphigus erythematosus, which frequently begins with an involvement of the nose with a lupus-erythematosus-like picture. Some of these lesions were covered with a scaly crust and resembled the type of lesion that one sees on the trunk with pemphigus erythematosus. I have never seen a lesion of this keratotic type on the nose. I think it would be difficult to make a definite diagnosis of pemphigus erythematosus for a lesion of this sort, but I feel that this is a more probable diagnosis than lupus erythematosus. One thing that I was not able to elicit from this patient was the history that the lesions clear quickly and then relapse. This patient has not had any sharp attacks of this sort, but in some cases of pemphigus erythematosus there is a great deal of variation in the intensity of the eruption on the nose from time to time. I feel that pemphigus erythematosus is a strong possibility, but I think that it is not possible to make a definite diagnosis.

DR JOHN F MADDEN, St Paul. I should like to ask whether the lesion was treated with solid carbon dioxide.

DR C W FINNERUD. I appreciate Dr Senear's discussion. I agree that it would be extremely unusual to have this syndrome limited to the nose for two and one-half years. However, I feel that pemphigus erythematosus is probably the correct diagnosis.

The treatment has consisted of both soothing and stimulating local preparations, a series each of injections of gold, sodium thiosulfate, typhoid vaccine and nicotinamide and arsenic by mouth in the form of arsenous oxide (arsenic) pills, all without improvement. One lesion was tested out therapeutically with roentgen rays, without improvement or aggravation, and another with solid carbon dioxide with the same result. I intend to try the suggestion of using a 40 per cent sulfur ointment locally and the other suggestion of giving acetarsone by mouth.

#### NEW YORK DERMATOLOGICAL SOCIETY

HANS J SCHWARTZ, M D, *President*

GEORGE C ANDREWS, M D, *Secretary*

*Oct 24, 1944*

#### Von Recklinghausen's Disease in Mother, Forme Fruste Type in Son and Daughter Presented by DR MAURICE J COSTELLO

E B, a woman aged 35 (private patient), has had a typical eruption of von Recklinghausen's disease since she was 12 years old. She had meningitis at the age of 10 and osteomyelitis of the long bones for twelve years thereafter. In 1934 she had an abscess of the left kidney, and she has had two miscarriages. She has difficulty in hearing with the left ear. During the past year the patient

complained of itching of lesions located on the head, back of the neck and upper part of the back

Her son, J W B, aged 11, has the forme fruste type of von Recklinghausen's disease. He has a number of cafe-au-lait spots on the trunk, varying in size from 0.5 to 3 cm. There are a number of round pea-sized, depigmented and hyperpigmented lesions which are slightly elevated above the cutaneous surface. He has a mild degree of stammering, and he is retarded in school.

Her daughter, E B, aged 3, also has the forme fruste type of neurofibromatosis. She is a normal child. She has a number of cafe-au-lait lesions on the dorsal aspect of the chest. Below and internal to the left scapula there is an elevated round deeply pigmented hairy lesion measuring 4 by 3 inches (10 by 7.6 cm). This is surrounded by an area of hyperpigmentation, and it is soft and transversed by what feel like sclerosed vessels. Roentgenograms of the spine do not show spina bifida.

#### DISCUSSION

DR RAY H RULISON: This is a fine demonstration. I agree with the diagnosis.

#### **Dermatitis Venenata from Rubber Gloves** Presented by DR EUGENE TRAUB

M M, a woman aged 51 years (private patient), was seen in February 1944, with a dermatitis of the hands. The exact cause was not determined with certainty, but rubber gloves were suspected of being a factor. The eruption disappeared with local management and no further trouble was experienced until one week ago, at which time the patient purchased an inexpensive pair of rubber gloves and wore them for approximately one hour while housecleaning. An immediate severe reaction, consisting of erythema and swelling of the hands, occurred. This was sharply limited at the wrist, marking the site of the top of the gloves. Within twenty-four hours tiny vesicles were profusely scattered over the entire dorsa of the hands, and in one or two sites small hemorrhagic blisters developed. A patch test performed with a portion of the rubber gloves and allowed to remain in place for forty-eight hours was strongly positive.

#### DISCUSSION

DR EUGENE TRAUB: This is the second patient recently seen with an acute dermatitis in which rubber gloves were proved to be the causative agent. The patient in a previous case was a worker in a chemical plant, and it was first thought that the chemicals handled were responsible for his dermatitis, but on patch testing the only positive reaction obtained was from his rubber gloves.

NOTE—The diagnosis was agreed on unanimously.

#### **Dermatitis Herpetiformis** Presented by DR FRED WISE

M G, a girl aged 4½ years, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on June 11, 1944, presented lesions of fifteen months' duration. A few itchy blisters appeared on the vulva a week after she was cured of chickenpox. She was admitted to Kings County Hospital, where she stayed for three and one-half months, during which time the eruption spread all over the body. She received a blood transfusion in September 1943. Within three weeks the lesions regressed but there was recurrence a week later. She was then hospitalized at the Cumberland Hospital for one year. She was treated with rectal injections of penicillin every three hours for five days and with local applications of penicillin salve, with no apparent improvement. She was later treated at the New York Post-Graduate Medical School and Hospital for three months. She received another blood transfusion. The lesions cleared up within two weeks but reappeared a week later. She was then treated with injections of 2 per cent solution of sodium arsenate, the dose beginning with 5 minims (0.31 cc) and being increased 2 minims (0.12 cc)

every other day, to 15 minims (0.92 cc) daily. Later, 0.4 Gm of sulfathiazole was given every four hours. One per cent solution of brilliant green was painted on the lesions. At present she is taking 0.25 Gm of acetarsone daily.

At the beginning the blisters are red and round with little white puncta in the center. After a few days they reach the size of a split pea. They become tense and cloudy and then rupture. They are at first discrete but later form into groups.

The lesions are located on the face, back of the neck, wrists, buttocks, upper third of the inner surfaces of the thighs and legs, pubic region and vulva. The initial lesion, seen on the inner surface of the right wrist, consists of a pinhead-sized reddish vesicle with a white punctum in the center and with a slight inflammatory halo around it.

The lesions consist of ill defined macules, vesicles and crusted patches on an erythematous base which are tender and painful to touch. They are discrete and aggregated, forming irregular patches. The largest patches are found on the inner surface of the thighs and the vulva. The lesions on the face are concentrated mostly on the forehead, tip of the nose, upper lip and chin and are heavily crusted and impetiginized.

The hemograms were normal except for 13 per cent eosinophils on June 14, 1944 and 4 per cent eosinophils and 14,400 leukocytes on July 27. Results of the chemical examination of the whole blood were normal on June 14, except for the elevation of the urea nitrogen to 17.5 mg per hundred cubic centimeters.

#### DISCUSSION

DR HOWARD FOX. I suggest the use of sulfapyridine. This has not yet been tried, but from my personal experience and from cases reported in the literature, it is certainly worth a trial.

#### **Hemangioma of Orbit with Cataract** Presented by DR GEORGE C ANDREWS

A M F, a girl aged 16 years, was admitted to Vanderbilt Clinic on Jan 1, 1944, for treatment of a hemangioma of the right upper lid and right side of the forehead. Two years previously she was told that she also had a cataract in this eye. She has never had roentgen ray or radium treatment.

Examination shows an extensive hemangioma as described. The lids of the right eye are swollen, and the eye is closed. The conjunctivas are chemotic and protrude through the closed lids. The bulbar conjunctiva is also chemotic. The cornea is roughened, the pupil is irregular and dilated, and there are posterior synechias. The lens is cataractous, and nuclear and subcapsular changes may be observed.

#### DISCUSSION

DR RAY H RULISON. This is an extremely interesting case because of the usual complaints of the use of radium to the eyes causing cataracts. This treatment has not been used in this case.

DR GEORGE C ANDREWS. This case is presented in order to record in the literature that spontaneous cataract has occurred in a case of angioma in which neither radium nor roentgen ray therapy was used. Considerable publicity was given to roentgen and radium cataract about eight or ten years ago. Personally, I have not seen radium cataract in any of the babies that I have treated for angiomas about the head or face. I have had only 1 case of cataract in an adult treated in 1928. However, I realize that radium treatment in the area about the eyes should be handled carefully, if at all. Sometimes, however, it is absolutely necessary to use radium near the eyes, as nothing else will effect a cure of extensive, bulky angiomatous involvement of the lids.

DR HOWARD FOX. Do you screen the eye when using radium? This is important for medicolegal reasons.



DR GEORGE C ANDREWS I always make an effort to protect the eye, but it is physically impossible to do so if radium is used anywhere near it because the radium rays spread about the shield and cause scattered rays to reach behind it. However, attempts are always made to protect the eye by inserting plates between the eyeball and the eyelid.

DR FRED WISE Angiomatous tumors are rare in adults. It is possible that in a patient aged 16 years some regression may still occur spontaneously.

DR GEORGE M MACKEE This case is of medicolegal importance. It is important to place on record a case of angioma of the eyelid, accompanied with a proved spontaneous cataract in a young person. Such cataracts when roentgen rays or radium have been used are blamed on the irradiation, in spite of the proved radio-insensitiveness of the eyeball.

The patient is an adolescent, the angioma is essentially one of the mucous membrane, and there has been no retrogression. That corresponds with my experience. It is my experience and opinion that angiomas of the skin usually undergo spontaneous involution before puberty, while those of the mucous membranes never improve spontaneously. Also, the latter do not respond favorably to safe doses of roentgen rays or radium, while those of the skin do respond favorably.

**A Case for Diagnosis (Dermatitis Herpetiformis, Impetigo Herpetiformis?)** Presented by DR FRED WISE

E D, a Negro woman aged 50, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Sept 11, 1944, presenting lesions of eight months' duration. She gives a history of recurrent attacks of bullous eruptions.

The lesions are numerous and generalized, including some on the scalp. They consist of bullae and heavy greenish-crusts, patches, most of which show a circinate arrangement. The primary lesion consists of a round, tense, lentil-sized vesicle containing a cloudy fluid.

The hemograms on three occasions were normal, with the eosinophils ranging from 1 to 3 per cent. The Wassermann and Kahn reactions, and results of mycologic examination and culture were negative. Patch tests elicited a 1 plus reaction to 30 per cent each of potassium iodide and potassium bromide in petrolatum.

From a histologic examination made by Dr Charles F Simms the eruption was diagnosed as dermatitis herpetiformis. The description follows: "At one end of the section there is a rather pronounced subepidermic edema which at several points has resulted in vesicle formation. Rather pronounced cellular infiltration is present in the upper part of the corium and is both perivascular and diffuse. The infiltration is composed of small round cells, wandering connective tissue cells, eosinophils, polymorphonuclear neutrophils and occasional plasma cells. In part, the section is covered with a crust."

DISCUSSION

DR PAUL E BECHET The presence of vesicles arranged in an annular and grouped manner and the lack of definite pustulation are, in my opinion, sufficient evidence to favor the diagnosis of dermatitis herpetiformis.

DR GEORGE M MACKEE I think that this is a case of dermatitis herpetiformis and not one of impetigo herpetiformis. The latter eruption occurs mostly, if not entirely, in pregnant women and in most instances is fatal. In this case there is grouping of lesions, but the elementary lesion is essentially a vesicle which later becomes pustular. There is subsequent crusting, but the crusted lesions do not resemble impetigo contagiosa, as they do in impetigo herpetiformis. Histologically, in the latter disease the pustule is in or immediately under the horny layer, while in this case the vesicle is much more deeply situated. Also, in impetigo herpeti-

formis there are more polymorphonuclears and more inflammation than are seen in this case

**Psoriasis Arthropathica** Presented by DR GEORGE M LEWIS

F C, a carpenter aged 58, removed a splinter from under the nail of his left ring finger twenty-seven months ago. Shortly afterward, there were swelling and pain in the region, followed by separation of the nail and, subsequently, inflammation of the region of the nail bed. Shortly afterward other fingers became considerably affected, the condition being confined to the region of the nail. During the course of treatment he received dressings which appeared to immobilize his hand. The rash spread up the fingers and affected his hand and forearm. This was later treated with wet dressings, with good response. No lesions have ever been present on his feet. At present, all the finger nails have been destroyed and all the nail beds are inflamed, showing redness, edema and some exudation. The fingers show limitation of movement, apparently amounting to ankylosis of the second interphalangeal joints.

The fingers also show considerable atrophy, apparently from disuse. The examination for fungi gave negative results.

NOTE—This case was previously presented at the Manhattan Dermatological Society, Jan 11, 1944.

**Psoriasis Arthropathica** Presented by DR GEORGE M LEWIS

J C, a white man aged 56, a retired meat packer, is presented from the New York Hospital. He has had psoriasis most of the time since it began twelve years ago. Treatment given or outlined by various physicians and at various clinics has been ineffectual for the most part. This has included roentgen ray therapy, low fat diet, autotransfusions and many prescribed or patent preparations for local use. During a visit to Florida, there was a temporary remission. Recently, new lesions have appeared, with a flare-up of the older lesions. During the past eight years, the patient has experienced progressive involvement of many different joints, with tender red swellings accompanied with pain. Typical lesions of psoriasis were present in the scalp, on the extensor surfaces of the arms and legs, on the buttocks and on the backs of the hands. The osteoarthritis involves the knees, ankles, spine and the terminal interphalangeal joints. Several finger nails and toe nails are thickened and yellow and are separated from the nail bed. The Wassermann reaction was negative, the urine normal and scrapings and cultures of the nails negative for fungi. A roentgenogram of his teeth showed areas of infection.

DISCUSSION

There was no discussion on the 2 foregoing cases.

**Multiple Osteomas** Presented by DR A BENSON CANNON

Mrs G O, a white housewife aged 58 years, was first seen on Sept 8, 1944, complaining of multiple, shotlike papules scattered over the sides of the face and forehead, of twelve to fifteen years' duration.

The past, family and personal history are irrelevant. The patient stated that these papules appeared grayish white in color and felt shotty when the cheeks were stroked with the hand. Rarely, one would become infected and discharge pus. The patient had consulted a number of physicians in Spain and in the capitals of Europe and was usually told by the examining physician that there was no cure. Most of the papules were removed with an electric needle by a physician in Barcelona, Spain, some fifteen years ago. They promptly recurred.

Examination reveals multiple, discrete, closely studded, grayish white papules in and beneath the skin of each side of the face, mostly on the cheeks. The papules vary from the size of a mustard seed to that of a split pea. They are hard

and raised and involve all of the layers of the skin. The surface over the papules is smooth. Hard, stony-like, grayish yellow particles can be picked out of each of the growths, leaving a small hole.

Biopsy of one of these removed lesions established that it was an osteoma.

Roentgenograms of the cheeks show multiple calcified nodules on the skin.

Treatment has consisted in the picking out of each of the calcified papules and five weekly doses of radiation, 100 r at each sitting.

#### DISCUSSION

DR HOWARD FOX: I should never have dreamed that these cutaneous lesions would contain deposits of bone. One would naturally suppose that the little hard, shotlike lesions were calcareous deposits in sebaceous cysts. However, this is an important case, and, for the sake of the record, I think Dr Machacek's findings should be corroborated by a general pathologist. It has been my impression that deposition of true bone in the skin was extremely rare.

DR GERALD MACHACEK: This is frank bone and not the first case of the sort I have seen. The first case report that I saw published was by Dr Hopkins, who observed the case clinically and got out myriads of little, round, white, ovoid lesions. The question is one of heteroplastic disseminated changes. I encountered 1 case, the report of which is to be published shortly, of congenital heteroplastic osteomas. The child in this case was born with these nodules.

The pathologic picture is one of bone osteoblasts with little fat cavities.

DR GEORGE C. ANDREWS: I had a case which, clinically, looked like the one presented. The patient was a woman of 35. The lesions resembled comedos. I took them out and found little pieces of hard material. A biopsy proved them to be bone. We also took dental roentgenograms which showed plainly that this material was bone.

DR ANTHONY CIPOLLARO: I have under treatment a Spanish woman about 60 years of age, who has an oily skin, milia and comedos. On occasion I removed what I believed to be milia and instead removed hard, irregular masses. Looking back now I realize that I had been removing small spicules of bone.

DR A. BENSON CANNON: This is the third private patient that I have had with lesions of this kind, the other 2 have had solitary lesions, and in neither instance did I make a clinical diagnosis. I hope to do better next time.

#### Psoriasis Beginning in Infancy Presented by DR EUGENE F. TRAUB

An eruption diagnosed as psoriasis in V. G., a boy aged 11½ years first developed when he was 1½ years old. There was a family history of the mother's brother also having psoriasis. The present eruption has been getting severer recently. This consists of warty lesions, particularly on the knees and fingers. Scattered over the body are typical punctate and guttate psoriatic lesions. The patient also has an interesting lesion involving the lip, which is definitely psoriatic in character and lies entirely within the vermilion border of the upper lip.

#### DISCUSSION

DR HOWARD FOX: The interesting feature in this case is that the history began when the child was 1½ years old.

DR A. BENSON CANNON: This is an unusual case of psoriasis. It would be of value to have a histologic report.

DR FRED WISE: Have any members obtained favorable results with sarsaparilla tablets?

DR EUGENE F. TRAUB: The reasons for presenting this patient were the early onset of psoriasis, at 1½ years, the lesions of the mucous membrane involv-

ing the vermillion border of the upper lip and the peculiar warty or vegetative type lesions found on the extremities. An attempt will be made to obtain a biopsy of the various types of lesions.

In answer to Dr Wise's question, I used sarsaparilla for a number of years, and in only 2 instances was there any improvement. I felt, however, that in the 2 cases in which improvement was noted this may have been coincidental to the therapy. In these 2 instances I felt that a spontaneous disappearance had occurred with the onset of summer weather. It is only fair to state that in my cases I used only a solution of sarsaparilla, without any local medication, as this would be the only way in which the therapy could be evaluated. My results were far different from those reported elsewhere in the literature.

### **Benign Pemphigus Presented by DR GERALD MACHACEK**

L P, a Negro woman aged 56, appeared at the Vanderbilt Clinic, presenting lesions, of over two years' duration on the neck, axillas, trunk, thighs, antecubital regions and scalp. These occur in repeated outbreaks and spread to the chest, armpits, abdomen, thighs and back. Attacks are intermittent, with scaling and painful irritation of the thighs and genitalia, which make walking impossible. It is worse in summer. Between attacks there is residual pigmentation.

The patient has had white hair since birth, and she has three children whose hair has been white since birth.

The lesions are widespread, symmetrically distributed and sharply demarcated, forming a complete collar involving the axillas and the inframammary, abdominal and inguinal regions. The areas are bullous, scaling and deeply pigmented (dark brown).

A biopsy of one of the lesions showed benign pemphigus.

Great improvement follows treatment with paste of zinc oxide with phenol.

### **DISCUSSION**

DR FRED WISE: This eruption seems to me to be an example of the Haley variety of familial pemphigoid.

DR MAURICE J COSTELLO: It is rare to find white hair in a full-blooded Negro at 50 years. When I questioned the patient about this condition she stated that her hair had been white since birth, as had that of her mother and several of her sisters and brothers. These facts are more interesting than the vesiculobullous eruption for which she was presented. The two conditions may be associated.

DR GERALD MACHACEK: I should like to stress the fact that similar conditions have been described before. McCarthy, in his text, mentions patients that have the bullae of pemphigus and dysperatosis of Darier. That is why I hesitated to call this the Haley type of pemphigus.

### **Sarcoidosis Presented by DR GERALD MACHACEK**

C R, a Negro woman aged 36 years, first appeared at the Vanderbilt Clinic in November 1937, with a history of having suffered for seven years from an eruption which was thick, raised and irregular and covered the lateral and anterior aspects of the nose as well as the external aspect of the septum. Small nontender lumps were present in the upper eyelids, the lips were slightly swollen and papules and comedos were present on both cheeks and the chin. The right hand was swollen, and a nodular infiltration 2 by 5 cm in diameter was present on the dorsum. All but the fifth finger were swollen, especially at the proximal phalangeal joints. The nails were eroded and striated. The left hand showed swelling of all fingers, with erosion of the finger nails. There was a raised, rough, crusted area, 2 by 2 cm, on the right elbow. There were diffuse areas of varying pigmentation on the back.

On March 28, 1938 regression of the cutaneous lesions was noted. On June 5, 1939 all lesions were said to have disappeared. On Dec 21, 1942 atrophic rhinitis, stenosis of the larynx and a deformity of the soft palate with adhesions to the posterior pharyngeal wall were interpreted as being of gummatous origin.

This case is presented as an instance of decided improvement of sarcoidosis in an American-born Negro woman who had stigmas of syphilis and had undergone antisyphilitic treatment.

A blood count showed 4,300,000 red blood cells, 3,840 white blood cells, 72 per cent hemoglobin and 73 per cent polymorphonuclear leukocytes. The erythrocyte sedimentation rate was 75 mm, and on June 16, 1941 it was 18 mm.

The serum phosphatase activity was 382 Bodansky units on Nov 4, 1937 and 139 Bodansky units on Nov 13, 1939.

On the patient's admission to the hospital, the Wassermann reaction was negative, on June 23, 1941 it was positive. On Sept 28, 1942, after she had received injections of bismuth, mercury and liver, the Wassermann reaction was negative. The patient had received antisyphilitic treatment in 1934.

On the patient's admission old tuberculin (1 10,000) elicited a negative reaction, on June 5, 1940, old tuberculin (1 100,000) elicited a positive reaction, on Sept 11, 1944, a dilution of old tuberculin, (1 10,000 and 1 1,000) elicited a positive reaction.

Roentgenologic examination showed sharply circumscribed, oval defects in the distal extremities of the proximal phalanges of both hands. On Sept 19, 1939, roentgenologic examination of both hands showed a generalized decrease in the size and distribution of previously reported areas of negative density. Some of the smaller defects had filled in completely.

Histologic examination showed sarcoid of the nose.

#### DISCUSSION

DR GEORGE C ANDREWS: Dr Machacek brought out an important point, illustrated by the 4 cases he has under observation, when he stated that as improvement occurs the patients with sarcoid become allergic to tuberculin.

DR EUGENE TRAUB: Is it not a fact that a positive reaction to tuberculin develops in the patient at a time when immunity is developing?

DR GERALD MACHACEK: This is not an isolated instance. I have seen 3 other cases in which the sarcoid disappeared and the tuberculin, which was negative at first, became positive.

DR HOWARD FOX: I do not think that the patient showed a specific reaction due to syphilis, and I doubt whether she ever had this disease.

#### A Case for Diagnosis (Erythema Multiforme Perstans?) Presented by DR JOHN C GRAHAM

Mrs M. R., aged 54 years last spring noticed for the first time red spots on her forearms, many of which have since coalesced. Later, similar lesions appeared on both sides of the neck and a few on the right shoulder. The rest of the body was unaffected. There was no itching or other sensation. The patient has been under my observation for the past two months, and during that time, except for a slight blanching of the lesions, there has been no appreciable change.

Each spot is a slightly elevated ring-shaped papule, varying in size from that of a split pea to several centimeters in diameter. The periphery of the papules is pink and elevated, and the center is violaceous and depressed. On the back of the forearm, near the elbow, the papules have fused and formed a single large area. Some of the papules suggest lichen planus, but this diagnosis was not borne out by a biopsy, which was performed on Sept 28, 1944, the description of which was as follows: "The epidermis is thin, and the surface is covered with

a thin layer of hyperkeratotic material. The rete pegs are absent or are extremely small, and a moderate number of cells in the deeper part of the epidermis show intracellular edema. In one tiny area the epithelial cells are degenerated. The corium is edematous, and the outer part shows small collections of round cells, some of which surround dilated capillaries and lymphatics. There are also areas showing proliferation of fibroblasts and numerous round cells, and a few pus cells and eosinophils are intermingled in these areas."

No diagnosis was made.

#### DISCUSSION

DR GEORGE M. MACKEE: I cannot accept the diagnosis of erythema multiforme perstans because there is no erythema while there is infiltration both clinically and histologically. Although the histology does not confirm it, there is a possibility of lichenoid leukemia. I cannot establish a diagnosis on the one microscopic slide presented tonight.

DR EUGENE TRAUB: A possibility that has not been mentioned is lichenoid sarcoid, but I do not know whether the plaque-like lesions could be made to fit into that picture. Granuloma annulare should also be considered, and I believe that this diagnosis could explain all the lesions found.

DR JOHN C. GRAHAM: I do not think that this is erythema multiforme but do not know what diagnosis to suggest.

#### Mycosis Fungoides (Tumor Stage) Presented by DR A. BENSON CANNON

S. R., a white truck driver aged 71, born in Rumania, first presented himself at the Vanderbilt Clinic in November 1943, complaining of pruritic lesions on the scalp, face, trunk and extremities for the past four years. He stated that he was well up to four years ago, when an itching eruption developed on the forearms, which later spread to the scalp and finally over the remainder of the body. He said that he had received roentgen ray treatments, with relief of itching and disappearance of those lesions. Some of these disappeared spontaneously. However, since he received the roentgen ray treatments, the last of which was given three years ago, the lesions have gradually reappeared, accompanied with the pruritus. They are not relieved by sunlight.

On examination, the lesions are found to be discrete, oval to irregular, circinate and gyrate, from 1 cm to 20 cm in diameter, rather sharply demarcated, elevated, infiltrated, erythematous and scaly. The lesions on the scalp are accompanied with areas of alopecia ranging from the size of a dime to that of a half-dollar. The elevated tumified lesions are on the forehead, on the cheeks and about the nose and lips. No lymph nodes are palpable. The finger nails are normal. There are no lesions on the glans penis. The heart, lungs, abdomen and reflexes are normal. The blood pressure is 100 systolic and 65 diastolic.

A blood count showed hemoglobin 13.8 Gm, red blood cells 5,050,000, white blood cells 7,600, polymorphonuclear leukocytes 79 per cent, lymphocytes 19 per cent, monocytes 1 per cent and eosinophils 1 per cent.

Roentgenologic examination of the chest showed no parenchymal infiltration or enlarged hilar nodes.

Examination of the lesions did not reveal fungi.

Biopsy specimens, taken from the edge of the lesions on the left shoulder and above the left eyebrow, were consistent with the diagnosis of mycosis fungoides.

Irradiation at the Vanderbilt Clinic has been of little value in controlling the development of the tumors. The patient was absent from the clinic for two months but returned with a large fungating, ulcerating tumor, about 5 cm in diameter, on the flexor surface of the left forearm.

#### DISCUSSION

All the members agreed with the diagnosis, and there were no comments.

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## DERMATOPHYTOSIS AND OTHER FORMS OF INTER- TRIGINOUS DERMATITIS OF THE FEET

A Comparison of Therapeutic Methods

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**B**OTH in civil life and in the armed forces, the control of those conditions of the feet which are commonly diagnosed as "dermatophytosis" has long been a problem. Even when "cured" they are likely to recur. They sometimes incapacitate. The incidence in college students is 50 to 70 per cent. Youth, hot climates and sweaty feet are predisposing factors. Today, in the army and navy, 8 per cent of hospital admissions in the United States are for dermatoses in general, and dermatophytosis ranks in incidence second only to contact dermatitis. In the foreign field the figure would doubtless be larger, and reports from the South Pacific area indicate that these dermatoses are outstandingly severe there. In short, there is acute need for a satisfactory means for keeping the feet of fighting men in good condition, in which connection intertriginous dermatitis poses a large problem.

At this point it is fitting to explain the relationship between "dermatophytosis" and "intertriginous dermatitis" mentioned in the foregoing paragraph. For a long time, some physicians have been jumping to the conclusion that intertriginous conditions of the toes, whether associated with lesions elsewhere on the feet or not, were due to fungous infection and were therefore dermatophytosis. This position was taken in spite of the fact that it was common knowledge that the fungi could not be demonstrated in many of the cases. One of us (F D W) pointed out as far back as 1927<sup>1</sup> that it was not reasonable that only fungi could cause intertrigo of the toes, and Mitchell<sup>2</sup> followed this up with an attempt to distinguish the cases of bacterial origin by clinical

From the Laboratory of Dermatological Research, University of Pennsylvania, assisted by a grant from the Council on Pharmacy and Chemistry, American Medical Association.

1 Weidman, F D. Laboratory Aspects of Dermatophytosis, *Arch Dermat & Syph* **15** 415 (April) 1927.

2 Mitchell, J H. Streptococcal Infection Simulating Ringworm of the Hands and Feet, *J A M A* **104** 1220 (April 6) 1935.

signs Recently, Hopkins and collaborators<sup>3</sup> have enlarged the idea They found that fungi could not be demonstrated in 30 per cent of their cases, even after repeated tests, and concluded on clinical grounds that dermatoses of the feet could be caused by hypostasis, minor trauma and sweatiness in addition to the bacteria and fungi In short, only part of the intertriginous types of dermatitis are dermatophytosis This indicates that physicians must be more discriminating if they would exhaustively evaluate dermatitis of the feet, at least when they enjoy the facilities (including laboratory) of civilian practice and military hospitals In the field, of course, it may be different The cases in which the condition is due to trauma, hypostasis and sweatiness will be the more readily identified, it is those due to bacteria that pose a real problem

It was with the full realization of the foregoing facts that we planned our studies at a penitentiary However, with our immediate interests related to the armed forces in the field, we did not attempt to discriminate among mycotic, bacterial and other intertrigoes We did exclude certain nonintertriginous conditions, such as callositas and the sodden plaques due to sweatiness to which Hopkins and collaborators<sup>3</sup> have called attention We included only those types of dermatitis which were conceivably due to bacteria or to fungi, especially if intertriginous, when there were lesions elsewhere which were of the nature of dermatophytosis, such as tinea cruris, they were included in the problem Nor did we attempt to differentiate rigidly between dermatophytosis and bacterial disease We adopted this policy because in the field the need is for a more or less blanket form of treatment, and, fortunately, a number of chemicals are available which are both antibacterial and antimycotic Incidentally, the same statements hold true in much of civilian practice

It is true that we conducted certain laboratory examinations, but they were only secondary to the larger purpose just indicated, treatment in the field They were made for what they might be worth later Thus, with scrapings available immediately and a rather full clinical picture in the record, the two might be found useful during the final analyses and prove to have significance with regard to some one of the therapeutic agents that we had employed Some of the results of these laboratory examinations will be discussed later in this paper, others will be reported more fully in further communications

The management of intertriginous infections as a whole resolves itself under three heads (1) prophylaxis, (2) treatment under close

3 Hopkins, J G , Hillegas A B , Camp, E , Ledin, R B , and Rebell, G Treatment and Prevention of Dermatophytosis and Related Conditions, Bull U S Army M Dept , June 1944, no 77, p 42



medical supervision in a hospital and (3) treatment without such supervision. As prophylactics, dusting powders containing boric acid, with or without salicylic acid, are the mainstays, but they are not invariably effective even when prescribed with directions for regular and conscientious use. Youth, by and large, is not likely to be systematic or conscientious, either to itself or to others, concerning the feet. It must be granted that foot baths containing sodium thiosulfate or sodium hypochlorite are theoretically indicated, but they are practical only in fixed quarters, such as cantonments and institutions, and even under such conditions there is a controversy as to their usefulness. In fact, certain controlled tests made recently in an industrial plant<sup>4</sup> throw grave doubt on their value. As to specific curative agents, dissatisfaction is general, particularly in respect to the recurrences that are so notorious. Thus far, salicylic acid, iodine and chrysarobin are the anchors, but the last two, particularly chrysarobin, are capable of producing a chemical dermatitis and hence should be employed only under expert medical supervision.

#### MATERIALS AND METHODS

With dermatophytosis as ubiquitous as it is, we confined our studies to prophylaxis and to treatment without close medical supervision in a hospital, indicated as points 1 and 3 in the preceding paragraph. Certainly, these aspects of treatment are most commanding both in the armed forces and in civil life, the great majority of infections are self treated until they force the patient to consult a physician. Medicaments were therefore selected that promised no untoward reactions when employed in the absence of close medical supervision. We were fortunate in our access to a penitentiary, because patients were under excellent control and available for follow-up study.

*Conditions of Tests* The studies were begun in November 1942 and continued into the late spring of 1943. That is, we were dealing with the "winter type" of infection, such as is commonest in the population at large regardless of season. Part of the buildings of the penitentiary are one hundred or more years old. Some of the floors of cells and corridors are wooden, but most of such floors have been replaced by stone or concrete. Bathrooms are spacious, with floors partly covered by wooden gratings. The entire institution is kept scrupulously clean and has adequate medical quarters and an excellent staff. Almost all the laundering is done by each inmate for himself in his cell with the result that even though stockings are not thoroughly sterilized in the laundry there is little likelihood that fungus is trans-

<sup>4</sup> Peck, S. M., Botvinick, I., and Schwartz, L. Dermatophytosis in Industry, *Arch. Dermat. & Syph.* 50:170 (Sept.) 1944.

mitted from patient to patient through stockings. Incidentally, we analyzed and compared the cases of infections originating in quarters having wooden, cement and stone floors, and we found no significant differences in relation to the various aspects of these intertriginous infections.

The inmates, all men, are largely "lifers," with an average age of 35 years. Of the group, 23.1 per cent are Negroes. There are not any requirements as to frequency of bathing, from the condition of their feet it appears that the subjects' hygiene is comparable to the average for the middle and lower classes of society. Naturally, we have checked carefully in respect to the credibility of the histories that have been given and have accepted or discounted each one *pro re nata*.

Records were kept on mimeographed protocols which included a diagram of the feet, on the latter, details as to the lesions were plotted. For the sake of uniformity, readings were made by one of us (F. D. W.) throughout, supplemented by conference with the other (F. A. G.) when it appeared advisable to check. In short, every effort was made to maintain uniformity in methods and standards of clinical readings. The necessity for such care cannot be overemphasized, obviously, the clinical observer who is dealing with scores of lesions cannot remember the multitudinous changes that occur over a period of weeks and months. We adopted a system of symbols for indicating the position, extent and type of lesion, these were plotted on the diagram. By the use of different-colored pencils in recording the symbols, the time factor was satisfactorily represented. By these means, a good perspective was secured, even months afterward, of the changes in the lesions, including the chronology.

Cultures were made for nearly all of the patients in order to learn later whether the species of fungus played any significant role in the premises. Scrapings were not examined under the microscope because the studies were directed primarily at the clinical aspects. The etiologic agent was important for the purposes of our study only in respect to the species (i. e., whether it was *Trichophyton interdigitale* or *Trichophyton purpureum*), a fact which cannot be determined by direct microscopic examination.

*Medicaments*—Six forms of medicaments were selected for trial. Two, Cresatin-Sulzberger and zephiran chloride are accepted as disinfectants by the Council on Pharmacy and Chemistry of the American Medical Association. Pomeio and Iodolate have not been thus approved. Ointment of benzoic and salicylic acid N. F. was included as a more or less "standard" therapeutic agent for dermatophytosis—that is, as a base line for comparison of results. A foot powder, 5 per cent boric acid in powdered talc, was selected as an additional "control," as we thought at first. However, we were agreeably surprised to learn

that it had high medicinal value and, accordingly, did not serve as the control anticipated. Fortunately, though, two of the six substances (Pomeio and zephiran chloride) eventuated as controls, because the lesions treated by them were not recognizably modified, they appeared to be inert.

*Description of Forms of Treatment* Patients under all plans of therapy were instructed to keep their feet clean and dry. The following six medicaments were employed as follows:

1 Cresatin-Sulzberger is metacresylacetate, manufactured by Sharpe and Dohme, Inc., Philadelphia. It is a colorless liquid, soluble in oils and alcohol but not in water. It has a strong odor resembling that of cresol. It was used full strength once or twice daily, in the case of the interdigital spaces, on a pledget of lamb's wool. We were led to the inclusion of this fungicide in our study because otologists had found it highly successful in treatment of otomycosis.

2 Boric acid foot powder. This consisted of 5 per cent boric acid in powdered talc. Incidentally, the army issue foot powder consists of salicylic acid 2 parts, boric acid 6 parts, zinc stearate 3 parts, exsiccated alum 1 part, starch 10 parts and powdered talc 78. It was dusted onto the feet three times a week.

3 Ointment of benzoic and salicylic acid N. F. A modified stock preparation of the penitentiary was employed (3 per cent salicylic acid and 12 per cent benzoic acid, with petrolatum as the base). It was rubbed in night and morning.

4 Iodolate (iodocholate) was employed in a 20 per cent ointment as supplied by the manufacturer. It was applied night and morning. It is manufactured by Iodocholate Products Corporation, Newark, N. J. It is brown and smells strongly of iodine.

5 Pomeio, manufactured by the Anderson-Stolz Corporation, Kansas City, Mo., is potassium mercuric iodide and was supplied by them in 12 per cent aqueous solution. It is colorless and odorless and contains enough alkali (25 per cent sodium hydroxide) to make it slippery to the touch. It was applied in the same manner as Cresatin.

6 Zephiran chloride is a water-clear, odorless liquid made by the Winthrop Chemical Co., New York. It is a mixture of alkyl dimethyl benzyl ammonium chlorides. It was used in 1 per cent aqueous solution in the manner described for Cresatin.

All the medicaments were applied by the prisoners themselves in their cells, assisted by mimeographed sheets of instruction. We inquired at each visit whether the treatment prescribed was being adhered to. If it was not, the patient was dropped from the study. In short, we did our best to have conditions in the penitentiary parallel those in private practice.

Treatment was not instituted until enough patients (117) had been assembled who were suitable as test objects and whose cultures had been identified. These were divided into 6 groups of 20, more or less, one group for each form of treatment. Subsequent defections of patients were made good by patients with comparably severe erup-

tions who became available later. Each group was reasonably uniformly composed in respect to kinds of lesions, that is, it contained similar numbers with "mild," "moderate" and "severe" eruptions, together with representatives of T interdigitale and T purpureum infection. These will be referred to as "original" tests. When it became clear (in two to three weeks) that Cresatin and the boric acid powder surpassed the other forms of treatment, we confined further tests largely to these two medicaments (patients were transferred from the groups treated with zephiran, Pomeio and the others). These further tests will be designated as "supplementary" tests. This explains why the results recorded herein concern a far greater number of experiences with these two medicaments than with the others, and why "experiences" ("original" plus "supplementary" tests) far outnumber the total number of patients in the entire series.

#### RESULTS

Under the heading of "Results" we feel justified in submitting certain (correlated) observations other than those immediately concerning treatment—namely, the role of the age of the patient, race and others. The patients were under such excellent control that the resulting data had unusual significance and merit recording. The breakdown appears in the following paragraphs. Throughout, it should be remembered that we were dealing with winter infections. The results which immediately concern the forms of treatment will be recorded first, thereafter the "correlated" findings will be dealt with.

*Evaluation of Medicaments*—Cresatin. At the outset 24 patients were tested ("original tests" in the table), the eruptions of 9 patients were cured, of 1 nearly cured and of 7 improved, 7 were stationary, and none was worse. There were not any complaints about the odor, we always inquired specifically on this point, but we realize that our clientele was not a fully representative cross section of American society. Incidentally, improvement was noted in 13 patients within a short time—namely two to three weeks, for others a period of four months was required. When the therapeutic response of patients receiving other forms of treatment, such as Pomeio and Iodolate, was found to be unsatisfactory, some of the patients were transferred to the group receiving treatment with Cresatin—45 in all. This created a supplementary group of therapeutic tests, but still within the original 117 patients. Of these, 7 were cured, 6 nearly cured, 21 improved, 9 stationary and 2 worse. The combined results of the 69 original and supplementary experiences with Cresatin were 16 cured, 7 nearly cured, 28 improved, 16 stationary and 2 worse. The table indicates these results, together with percentages. There was only one untoward

reaction, it appears, late in the course of treatment the patient stated that the substance burned him. We could not examine him until one month later and could not check his statement objectively. In short, Cresatin made an excellent showing.

**Boric Acid Powder** For the sake of brevity, we designated this "hygienic" treatment. Twenty patients were tested at the outset (original tests in the table), and, as in the case of Cresatin, a second group (supplementary experiences) was also tested as the result of transfers from other forms of treatment. The results were as follows. In the "original" group, 6 patients were cured, 3 nearly cured, 1 improved, 7 stationary and 3 worse. Ten of the 20 were at least improved after two or three weeks. In the "supplementary" group (29 in all), 10 were cured, 1 nearly cured, 12 improved, 5 stationary and 1 worse. The combined results for the two groups (a total of 49 experiences with "hygienic" treatment) were 16 cured, 4 nearly cured, 13 improved, 12 stationary and 4 worse. Here, again, an excellent showing was made. Both for Cresatin and for the boric acid powder, the consistently favorable comment of the patients confirmed the results arrived at on paper. There were no untoward reactions.

**Ointment of Benzoic and Salicylic Acid N F** Sixteen patients were tested in the "original" group. Four were cured, 2 nearly cured, 8 improved, 1 stationary and 1 worse. In the "supplementary" group, 9 in all, 1 was cured, none nearly cured, 3 improved, 3 stationary and 2 worse. The combined results for the two groups (25 experiences) were 5 cured, 2 nearly cured, 11 improved, 4 stationary and 3 worse. In general, this ointment was useful in the earlier stages of our particular series of winter infections, but it stopped short of achieving cure. There were no untoward reactions.

**Iodolate** Twenty-one patients were tested. The showing was fairly creditable in respect to therapeutic improvement, 3 cured, 1 nearly cured, 8 improved, 3 stationary and 6 worse. However, the percentage figure (28.5) of "worse" patients, which is bad enough, was accentuated by the severity of the untoward reactions, which were suppurative. In 3 patients a chemical dermatitis promptly developed. Moreover, a positive reaction resulted from patch tests employed on 2 of the "worse" patients. Accordingly, it was not tested further than in the original group of 21 patients, and a "supplementary" set of tests does not therefore appear in the table. Judged by our experiences, the preparation requires close medical supervision, and, moreover, is not equal therapeutically to certain other forms of treatment that we employed.

**Pomeio** Eighteen patients were included in the group. Two were cured, none nearly cured, 6 improved, 2 stationary and 8 worse. In short, this preparation was decidedly inferior in our hands. Untoward

reactions were practically nil, at most, 3 patients exhibited superficial maceration which may have been referable to the alkaline nature of the preparation. They did not report any subjective symptoms.

**Zephiran Chloride** Eighteen patients were employed. It became clear at the first examination (at the end of three weeks) that it was inferior to cresatin and "hygienic" treatment, and later it was found to be inferior in general under the circumstances of our tests. Eventually 1 patient was cured, 1 was nearly cured and 4 were improved, 8 were stationary, and 4 were worse. Moreover, the results were no better at the end of six weeks. There were no untoward reactions.

*Results of Tests (117 Patients, 200 Experiences)*

Patients in original group	Benzoic Salicylic Acid						Totals
	Cresatin 24	Hygienic 20	Ointment 16	Iodolate 21	Pomeio 18	Zephiran 18	
<b>Cured (A)</b>							
Original tests	9	6	4	3	2	1	25
Supplementary	7	10	1	0	0	0	18
Total experiences	16-23 1%	16-32 7%	5 20%	3 14 2%	2 11%	1 5 5%	43 21 5%
<b>Nearly cured (B)</b>							
Original tests	1	3	2	1	0	1	8
Supplementary	6	1	0	0	0	0	7
Total experiences	7 10 1%	4 8 1%	2 8%	1 4 7%	0-0	1 5 5%	15 7 5%
<b>Improved (C)</b>							
Original tests	7	1	8	8	6	4	34
Supplementary	21	12	3	0	0	0	36
Total experiences	28-40 5%	13 26 5%	11 44%	8-38 1%	6-33 3%	4 22 2%	70 35%
<b>Stationary (D)</b>							
Original tests	7	7	1	8	2	8	28
Supplementary	9	5	3	0	0	0	17
Total experiences	16 23 1%	12 24 4%	4 16%	3 14 2%	2 11%	8-44 4%	45 22 5%
<b>Worse (E)</b>							
Original tests	0	3	1	6	8	4	22
Supplementary	2	1	1/2	0	0	0	5
Total experiences	2 2 9%	4 8 1%	3 12%	6-28 5%	8-44 4%	4 22 2%	27 13 5%
<b>Total experiences</b>	<u>69</u>	<u>49</u>	<u>25</u>	<u>21</u>	<u>18</u>	<u>18</u>	<u>200</u>
<b>Totals of favorable results</b>							
A + B =	33 2%	40 8%	28%	18 9%	11%	11%	
A + B + C =	73 7%	77 3%	72%	57%	44 3%	33 2%	

COMMENT ON MEDICAMENTS

As shown by the totals at the bottom of the table, and considering the results for only the "cured" (A) and "nearly cured" (B) patients because they are the most unequivocal, Cresatin and "hygienic" (boric acid powder) treatments stand far ahead of the others. When the results for "improved" patients (C in the table) are added to these (A + B + C), ointment of benzoic and salicylic acid N. F. enters the picture. Now the results are singularly uniform—73.7 per cent for Cresatin, 77.3 per cent for boric acid and 72 per cent for the ointment. In other words, all of these 3 forms of treatment resulted in improve-

ment (or better) in about three quarters of the cases. It also shows that ointment of benzoic and salicylic acid shifts the results in our table toward improvement but does not make a good showing in respect to cure. By way of supplementing this evaluation, the table may be studied from the reverse direction—namely, of poor (“worse”) results. Now it is noted that less than 3 per cent of the patients became worse under treatment with Cresatin, thus decidedly strengthening its showing.

It is clear from the table that Cresatin and hygienic treatments made the best showings and were nearly equal in value. However, there are several considerations which cannot appear in the table because we could not reduce them to statistics but which must be given weight in a final evaluation. We refer to the promptness in the therapeutic response to Cresatin, the absence of untoward reactions and the personal satisfaction of patients with this medicament. In short, considering all factors in the situation—statistical, clinical impressions and patients’ opinions—we feel that there is a certain balance of evidence in favor of Cresatin over the boric acid powder.

Hygienic (boric acid powder) treatment, besides producing favorable results in our patients, raised the question of the preference for powders over other forms of agents, particularly in view of their associated drying powers and convenience of applications. This led to a second series of tests, at another penitentiary, wherein Cresatin was exhibited in powder as well as in liquid form. The results will be reported fully elsewhere. Suffice it to record here that results were disappointing. Incidentally, in this second set of tests, Cresatin (liquid) was found superior to the hygienic treatment, which was again tested for control purposes.

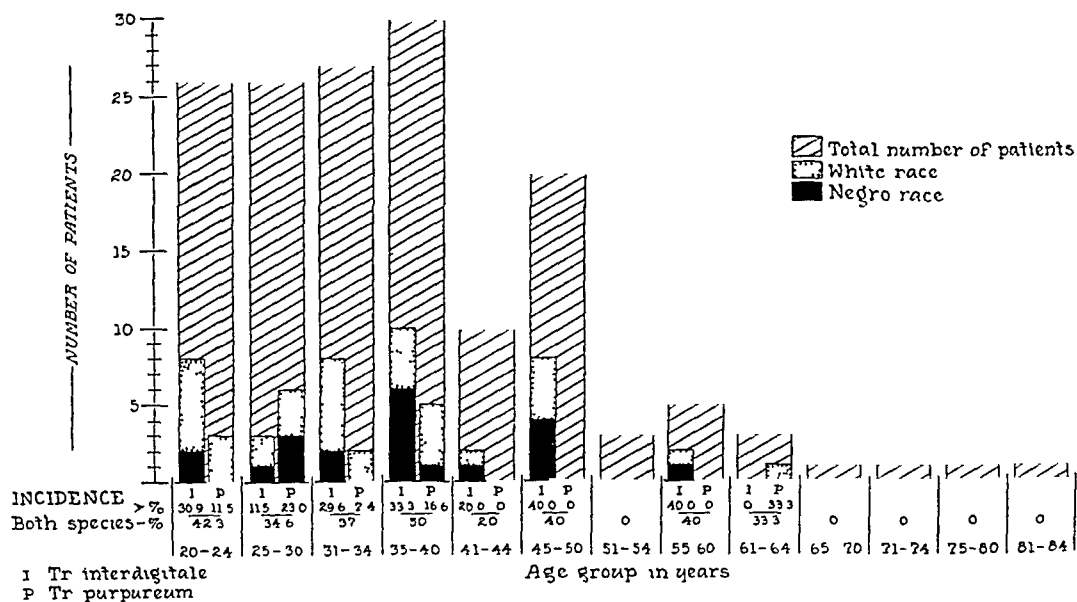
Confirming our previous clinical impressions, ointment of benzoic and salicylic acid tended to result in improvement only up to a certain point, i. e., short of the disappearance of hyperkeratosis. This was the case at both of the penitentiaries.

#### SUPPLEMENTARY OBSERVATIONS

In addition to the foregoing evaluation of medicaments our data supplied information concerning certain other aspects of intertriginous infection. Some required such extensive reports that they will appear in separate, subsequent communications, but the ones requiring less extensive discussion will be recorded forthwith. We have analyzed our records in several directions, but only those findings that appear to have significance will be recorded. Once again, they should be regarded only in the light of winter infections. The basis for computations in the several phases of the data (age, race, species of culture, etc.) will be found to vary because we took advantage of the larger

figures that were available in some circumstances than in others. Thus, where the factor of treatment entered the picture, we were confined to the data on 117 cases, but the data were larger when only race, age and cultures were concerned because we were able to include some of the patients who did not persist in the treatment prescribed and were dropped.

*Age*—The average age of 154 patients was 35 years. The youngest was 20 years old. Only 10 per cent were older than 50. Prior to age 50, the several age groups were evenly distributed, that is, there was not any preponderance of patients around age 25, age 30, etc., with the exception of one group. Thus, there was a striking scarcity of cases from age 41 to 44 which we cannot explain. After age 50, there was a striking decrease in incidence.



Species of fungi in relation to age and race, occurrence of 58 cultures from 154 patients. (The 1 culture of *Epidermophyton inguinale* that was secured is not represented in this chart, this fact will account for an apparent discrepancy between the percentages in the chart and certain ones in the text.)

As to cultures, prior to age 41, growth was secured from 42 per cent of the patients, after age 41, from 20 per cent. *T. purpureum* infections fell preponderantly in the years prior to middle life (16 of the 17 cases). After age 40, there was only 1 example of *T. purpureum* infection but there were 12 examples of *T. interdigitale* infection. The ratio of infections due to *T. purpureum* to those due to *T. interdigitale* was 1:2 prior to age 41 but only 1:12 after age 40. That is, prior to age 41, *T. purpureum* infections were found to occur about six times as frequently as *T. interdigitale* infections. To sum up, whereas *T. interdigitale* remains the most frequent species when considered for



all ages, the earlier years appeared to predispose to *T. purpureum* infection in our patients.

As to severity of lesions, our data were significant as to age only in that severe infections occurred more frequently in age group 35 to 50, middle life. For this we have no explanation.

*Race* Race had a clearcut relationship to the mycology in the case. As to frequency of culture, a total of 154 patients, both Negro and white, yielded 59 positive cultures (38.3 per cent). Twenty-one of 41 Negro patients gave positive cultures (51.2 per cent), and 38 of the 113 white patients yielded positive cultures (33.6 per cent). This ratio of 51:33 has significance. Among the Negroes, *T. interdigitale* occurred seventeen times and *T. purpureum* only four. This gives a ratio of approximately 4:1 among them, whereas the ratio in the white patients was 2:1, as may be seen from the chart. In other words, *T. purpureum* was encountered twice as frequently in white patients.

As to types of lesions, only two appeared to have significance in respect to race. The hyperkeratotic one ("soft corn") occurred sixfold more frequently in the Negro race. Plantar vesicles were three times more common in Negroes.

*Type of Lesion* Scaliness was observed in the large proportion of cases that might be expected. Maceration appeared in about half of the cases, whether the lesions were simply scaly or were hyperkeratotic. Newly developed plantar vesicles appeared in about 16 per cent of the patients, the remains of vesicles in 6 per cent. Hyperkeratotic lesions were represented between the toes in 24 per cent. The "purpureum" type of dermatophytosis recently identified by Lewis<sup>5</sup> was represented clinically in about 7 per cent of the patients—on the ankles, instep and soles. Only 3 cases of frankly eczematoid dermatoses were included in our experience.

These different types of lesions have been analyzed in respect to (1) species of fungus concerned, (2) race and (3) effectiveness of treatment, with results as follows:

As to the fungi in the case, from macerated lesions cultures were secured in 44.4 per cent of the attempts, as against 37.9 per cent for lesions as a whole, the proportion of *T. interdigitale* to *T. purpureum* was the same as for lesions as a whole.

For hyperkeratotic lesions (without maceration), the statistics pointed the same way as for macerated lesions, but even more emphatically in one respect. Thus, cultures were secured in a larger number of attempts (57.1 per cent), the ratio of *T. interdigitale* to *T. purpureum* remained the same as for lesions as a whole.

<sup>5</sup> Lewis, G. M., Montgomery, R. M., and Hopper, M. E. Cutaneous Manifestations of *Trichophyton Purpureum* (Bang), *Arch. Dermat. & Syph.* 37:823 (May) 1938.

From vesicular lesions, cultures were secured in the same ratio of frequency as for the entire series of lesion types, but there was a great preponderance of *T. interdigitale*, the ratio was 5:1, as against the expected ratio of about 2:1 when based on all classes of lesions. In short, *T. interdigitale* occurred 2.5 times as frequently in vesicular lesions as in lesions in general. This tends to support Lewis' <sup>5</sup> thesis that *T. interdigitale* induces an acute type of infection.

As to the relationship of race to particular types of lesions, hyperkeratosis occurred seven times more frequently in Negro patients. Maceration occurred nearly twice as frequently in the Negroes, plantar vesicles three times as frequently. We did not analyze scaliness in detail, because it is common to nearly all lesions, nor fissuring, because it varies so rapidly in the same patient. The number of patients with lesions of "purpureum type" (see Lewis <sup>5</sup>) was so small (only 9) that it was inadequate for analysis.

As to the selectivity of one particular form of treatment for a particular type of lesion, conclusions are not permissible because so many medicaments were tested (6) that the results of analysis could not be significant, obviously, only a few of each type of lesions would receive a given form of treatment. However, some information was secured that was at least suggestive when the analysis was based on several forms of treatment. Incidentally, results of treatment were here evaluated on the basis of both "cured" and "almost cured" infections, on the one hand, and on "worse" infections on the other, infections that were simply "improved" were not included because they are so equivocal. In the foregoing circumstances, hyperkeratotic lesions were twice as refractory to treatment. Macerated lesions responded *pari passu* with lesions as a whole, but there were few indeed that became worse at any time. In fact, a large bulk of "improved" lesions makes it appear that macerated lesions responded in general more favorably than the average. Plantar vesicles responded best, 41 per cent were cured or almost cured, against an average of 28 per cent for all cases. In short, vesicular and macerated lesions cleared the most satisfactorily, while hyperkeratotic ones were the most resistant.

*Comparison of T. Interdigitale and T. Purpureum in Relationship to Types of Lesions Produced and Cure*—Lewis <sup>5</sup> has asserted that a distinctive type of dermatitis is induced by *T. purpureum* and that it is more resistant to treatment than that produced by other organisms. We regret that we cannot confirm his thesis in its entirety, because it would mean a long step in advance in the prognosis and treatment of dermatophytosis. At the same time, we cannot quite dispute one part of it, namely that *T. purpureum* produces a distinctive type of lesion, because we realize that we have not acquired the proficiency

that he has in these premises and did not have so large a number of cases for study. In any event, of nine diffuse and subacute lesions involving the ankles, which we interpreted as of Lewis' *T. purpureum* type, we isolated *T. interdigitale* from 3 and *T. purpureum* from 1, the other 5 were negative for fungi. Moreover, *T. purpureum* occurred in severe infections (meaning extensive or acute) twice as often as *T. interdigitale*.

However, we can speak definitely in the matter of treatment because the personal equation is not involved in the identification of cultures or the recognition of cure. Unlike Lewis, we found that 50 per cent of the infections caused by *T. purpureum* were cured, contrasted with 32.4 per cent of those due to *T. interdigitale*. To sum up, the findings of Lewis were not confirmed in this penitentiary, particularly as to the resistance of *T. purpureum* to treatment. Perhaps the factor of winter dermatophytosis accounts for part of this discrepancy.

#### SUMMARY AND CONCLUSIONS

Under the excellent control and uniformity of conditions of a penitentiary, 117 inmates having winter dermatophytosis were selected as test objects for six different forms of treatment. Of these, meta-cresylacetate (Cresatin) is regarded by us as superior, but a simple boric acid powder was almost as efficient.

Response to treatment was poorest in hyperkeratotic lesions and best in vesicular and macerated ones.

Lesions caused by *T. purpureum* were not particularly distinctive and were not more resistant to treatment than other lesions.

Negroes were far more liable to hyperkeratotic and to macerated lesions and to plantar vesicles.

A remarkably high percentage (37.9) of positive cultures was secured, although only one attempt was made for each patient. They were obtained twice as frequently prior to age 41, were obtained far more frequently from Negroes (51.33) and were secured from 57 per cent of the hyperkeratotic lesions. *T. interdigitale* was, as usual, by far the commonest species. Infections due to *T. purpureum* were confined, almost entirely to years prior to middle life and occurred twice as frequently in the white race. *Epidermophyton inguinale* was isolated only once. The type of lesion appeared to influence the percentage of positive cultures secured, both hyperkeratotic and macerated lesions were outstanding. They yielded 50 per cent and 100 per cent more positive cultures than the average. We submit these data in respect to cultures in the sense only that they indicate the circumstances at a particular penitentiary. They cannot be representative for dermatophytosis at large.

## PENICILLIN OINTMENT IN THE TREATMENT OF SOME INFECTIONS OF THE SKIN

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MANY reports from English and American investigators indicate that local applications of penicillin are useful in the treatment of pyogenic infections of the skin. Bodenham<sup>1</sup> found that a penicillin cream was effective in eliminating streptococci and staphylococci from burns and surface wounds. Roxburgh, Christie and Roxburgh<sup>2</sup> prepared a penicillin ointment and a penicillin spray. They reported that local applications of penicillin were effective in the treatment of sycosis barbae and impetigo. Taylor and Hughes<sup>3</sup> applied penicillin ointment and penicillin in a spray to lesions of impetigo, sycosis barbae and furunculosis, with favorable results. Sophian and Connolly<sup>4</sup> treated acute and chronic pyogenic infections of the skin with a penicillin ointment containing a wetting agent. The results were good, especially in furunculosis and sycosis barbae. Schoch<sup>5</sup> applied the washings of "empty" penicillin ampules to the lesions of 4 patients with diseases of the skin and was enthusiastic as to the results. Johnson<sup>6</sup> prepared an ointment contain-

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Studies, observations and reports from the dermatologic departments of the Barnard Free Skin and Cancer Hospital and Washington University School of Medicine (Service of Dr. M. F. Engman Sr.)

1 Bodenham, D. C. Infected Burns and Surface Wounds. The Value of Penicillin, *Lancet* **2** 725 (Dec. 11) 1943.

2 Roxburgh, I. A., Christie, R. V., and Roxburgh, A. C. Penicillin in Treatment of Certain Diseases of the Skin, *Brit. M. J.* **1** 524 (April 15) 1944.

3 Taylor, P. H., and Hughes, K. E. A. Infective Dermatoses Treated with Penicillin, *Lancet* **2** 780 (Dec. 16) 1944.

4 Sophian, L. H., and Connolly, V. J. The Use of Penicillin in Topical Application, *Am. J. M. Sc.* **208** 577 (Nov.) 1944.

5 Schoch, A. G. Local Penicillin Therapy, *Arch. Dermat. & Syph.* **50** 202 (Sept.) 1944.

6 Johnson, H. M. Penicillin Ointment for Piodermas, *Arch. Dermat. & Syph.* **51** 270 (April) 1945.

ing penicillin and found that it was effective in the treatment of certain pyogenic infections of the skin. Templeton, Clifton and Seeborg<sup>7</sup> found that penicillium gauze, solutions of crude penicillin and purified penicillin in ointment bases were valuable therapeutic agents in the treatment of pyogenic infections of the skin. Cohen and Pfaff,<sup>8</sup> using penicillin by injection and penicillin ointment, obtained satisfactory results in 100 cases of pyogenic infections, including impetigo, sycosis barbae and "so-called" tropical ulcer. Wrong<sup>9</sup> treated 93 patients with cutaneous infections with a penicillin ointment and also reported excellent results in impetigo and sycosis barbae, although relapses were frequent in cases of sycosis barbae.

We treated 48 patients with pyogenic infections of the skin with penicillin ointment. The ointment was made with sterile materials under aseptic conditions. The ointment base was water miscible and contained glyceryl monostearate, stearic acid (U S P), Duponol, a preservative (propyl ester of parahydroxybenzoic acid in a concentration of 0.08 per cent) refined peanut oil and distilled water. The peanut oil was added to prevent caking and drying on application. The  $p_H$  of this ointment was approximately 6.5. Penicillin sodium (commercial, Chas. Pfizer & Company, Inc., Brooklyn) which had been pretested by the United States Food and Drug Administration was added to the base in a concentration of 500 Oxford units per gram. When tested by the Standard Food and Drug Administration method for antiseptic ointments, this penicillin ointment gave a zone of penetration of 16 mm with *Staphylococcus aureus*. The penicillin sodium contained in the ointment was stable to a high degree for a period of at least six months at refrigerator temperature (below 10°C).

Before treatment was begun cultures were obtained from almost all the patients. The patients were directed to keep the ointment in a refrigerator when not in use. At first, directions were given to apply the ointment seven to eight times a day. Later, a few patients were directed to apply the ointment four times a day. The results appeared to be about the same in both groups, so that most of the patients were told to apply the ointment four times a day.

#### DISEASES TREATED

*Impetigo* Twenty-one patients with impetigo were treated by local applications of the penicillin ointment. *Staph. aureus* was found

7 Templeton, H. J., Clifton, C. E., and Seeborg, V. P. Local Application of Penicillin for Pyogenic Dermatoses. *Arch. Dermat. & Syph.* **51**: 205 (March) 1945.

8 Cohen, T. M., and Pfaff, R. O. Penicillin in Dermatologic Therapy, *Arch. Dermat. & Syph.* **51**: 172 (March) 1945.

9 Wrong, N. M. Penicillin Therapy in Skin Infections, *Canad. M. A. J.* **52**: 341 (April) 1945.

on culture from all but 3 of these patients. The reports on cultures for these 3 were *Staphylococcus albus*, diphtheroids and no growth, respectively. The most favorable results were obtained in this group of patients. Thirteen patients were cured. The average length of time to complete the cure was 5.8 days. Six patients were decidedly improved in an average of 7.5 days. Many of these patients did not return for follow-up visits. In 2 of the patients a contact dermatitis developed during treatment. This was noted five days after treatment was begun in 1 case and fourteen days after treatment was begun in the other. This will be discussed in detail later.

*Secondary Infections*—A group of 17 patients with secondary infections of the skin were treated with the penicillin ointment. The eruptions might be classified as pyodermas. Included were 4 patients with acne vulgaris with large pustules of the face, 3 with nummular eczema in which the eczematous lesions were studded with pustules and 2 with pemphigus with pustular lesions on the body, others had infections following burns, and 1 had herpes simplex of the face. *Staph aureus* was found on culture in 10 cases, *Staph albus*, in 6 cases, and a contaminant, in 1 case. The secondary infection responded to treatment with the ointment, although the length of time necessary to produce improvement was much longer than for impetigo. The average duration of treatment was 22.5 days. In 1 case treatment was classified as a failure, and in 1 case contact dermatitis was noted seven days after treatment was begun.

In most of the cases treatment was instituted for the original disease after the infection improved.

*Sycosis Vulgaris*—Five patients with sycosis vulgaris were treated. Cultures were reported as yielding the following organisms: *Staphylococcus albus* (2), *Staph aureus* (1), diphtheroids (1), and no growth (1). Three of the patients responded favorably. In 1 of these persons the eruption tended to recur. Two relapses were treated in this patient with favorable results. Two patients responded to treatment, but a contact dermatitis developed in three days in one and in fifteen days in the other following the beginning of treatment.

*Miscellaneous Infections of the Skin*—After thirty-six days of treatment, 1 patient with furunculosis was improved. One patient with a recurrent pustular eruption of the hands and feet was not improved after seventeen days of treatment. A patient with an infection of the hand and lymphangitis of the arm was improved after the hand had been treated for two days with hot soaks followed by the ointment. This patient did not return for observation after the second visit. A white woman, for whom a diagnosis of pyoderma faciale<sup>10</sup> was made, was

10 O'Leary, P. A., and Kierland, R. R. Pyoderma Faciale, Arch Dermat & Syph 41 451 (March) 1940.

treated and cured in twenty-eight days<sup>11</sup> A patient with a staphylococcic dermatitis was improved in seven days

#### REACTIONS TO TREATMENT

Contact dermatitis developed in 5 of the 48 patients (10.4 per cent) while they were being treated with the penicillin ointment. The contact dermatitis was characterized by erythema, edema and vesicles in some of the patients. The dermatitis appeared in from three to fifteen days after the beginning of the treatment and cleared promptly when treatment was stopped. Two of the cases are reported in detail.

#### REPORT OF CASES

CASE 1—L. A., a 52 year old white man, on Feb. 12, 1945 complained of an eruption about the nose of three days' duration. This followed an attack of influenza. Examination revealed a vesicular and pustular eruption on the upper lips and cheeks about the nose. The diagnosis was secondary infection of herpes simplex. A culture of the lesions revealed *Staph. albus*. He was given the ointment and instructed to apply it five or six times a day.

On February 13 there was much improvement in the pustular lesions.

On February 19 an erythematous and vesicular eruption was noted which involved the lower two thirds of the face and the eyelids. Use of penicillin ointment was discontinued, and the patient was instructed to apply cold towels every hour.

On February 22 there was some improvement in the dermatitis of the face.

On February 24 the dermatitis was nearly well.

CASE 2—J. F., a 53 year old white woman, on May 26, 1945 complained of an eruption of the face of about four days' duration. Examination revealed a typical impetigo involving the sides of the face and the chin. The organism cultured was *Staph. aureus*. She was given the penicillin salve to apply four times a day.

On May 28 the old lesions were improved, but there were a few new lesions.

On May 31 the patient complained of severe itching of two days' duration. Examination revealed an erythematous and scaling eruption of the sides of the face with some swelling of the face. The impetigo was improved. The use of penicillin ointment was discontinued, and the patient was instructed to apply cold towels.

On June 1 the dermatitis was much improved.

On June 4 the dermatitis had completely disappeared. Two small areas of impetigo remained.

The impetigo cleared in a few days after application of ammoniated mercury ointment.

#### PATCH TESTS

Of the patients in whom contact dermatitis developed during treatment, 2 were available for patch tests. The patch tests were performed in the following manner:

Three samples of commercial penicillin sodium dissolved in isotonic solution of sodium chloride (10,000 units per cubic centimeter) were applied to gauze and

<sup>11</sup> This patient was observed six months later and had not had any relapse.

placed on the skin. Saline solution was used as a control and applied in the same manner. The ointment base and peanut oil (as used in the ointment) were applied to patches of gauze and placed on the skin.

Positive reactions to all the patches with penicillin were observed, with erythema and edema in 1 patient and vesicles in the other. Negative reactions were observed to the saline solution, the peanut oil and the ointment base. In 1 of the patients a flare-up at the site of the previous contact dermatitis was observed after the patches had been applied.

#### COMMENT

The penicillin ointment which we used in our clinical trials was developed after extensive studies of ointments. It was chosen because of the stability of the penicillin in the ointment and because the release of penicillin from this type of ointment was found to be greater than from other types of ointments. Our clinical studies have shown that penicillin in this ointment is effective in the treatment of certain staphylococcal infections of the skin. The best results were obtained in the treatment of impetigo. Almost all the patients with this disease were cured. Decided improvement was noted after its use against furunculosis. One of the patients treated for sycosis vulgaris had several relapses, but each relapse was adequately controlled with the ointment. Secondary cutaneous infections accompanying certain other diseases of the skin were treated and were for the most part improved. No studies were done to determine whether or not the organisms involved became resistant to penicillin.

Patch tests on 2 of the patients in whom contact dermatitis developed during treatment gave us valuable information as to the antigenic agent of the contact dermatitis. These 2 patients were found to be extremely sensitive to patch tests with three separate batches of the penicillin sodium (dissolved in isotonic solution of sodium chloride). Other investigators who used penicillin locally have reported contact dermatitis in certain patients. Patch tests have been used by some of them. Cohen and Pfaff found that 5 patients of their series were sensitive to penicillin, 4 of them presenting an acute reaction to the drug after application. They performed patch tests with the ointment and found that 0.95 per cent of 524 subjects reacted to it. Wrong made patch tests with a "penicillin emulsion" and found that positive reactions developed in 2 patients who had had a dermatitis after local application of this "penicillin emulsion". The "emulsion" itself was used as a control, with negative results. We know that contact dermatitis can develop in people who handle penicillin and its salts. Pyle and Rattner<sup>12</sup> reported the first case and

<sup>12</sup> Pyle, H. D., and Rattner, H. Contact Dermatitis from Penicillin, *J. A. M. A.* **125** 903 (July 29) 1944.



observed positive reactions to penicillin patch tests with itself. Silvers<sup>13</sup> performed patch tests on a chemist who had acquired a dermatitis while handling amorphous penicillin and observed a positive result.

Our clinical impressions after we have used penicillin ointment for several months are these. While impetigo cleared up with penicillin ointment the results are no better than when ammoniated mercury or bismuth tribromophenate (xeroform) are used. Sycosis vulgaris is definitely improved in some cases when penicillin ointment is used, but the results do not appear to be any better than those obtained with the use of compound ointment of oxyquinoline sulfate. From the limited studies thus far made, in treatment of secondary infections penicillin ointment does not appear to produce any better results than the older antiseptics. Since the percentage of reactions to penicillin salve is relatively high and some of the reactions are rather severe, we feel that this drug may prove to be less useful in the treatment of cutaneous infections than some of the older antiseptics. The product seems to produce improvement somewhat faster than the older drugs, but this does not overcome the advantage of the older drugs from the standpoint of stability, availability and cost.

#### CONCLUSIONS

1 The penicillin ointment which was used in our clinical trials was effective in the treatment of certain pyogenic infections of the skin. It was most effective in the treatment of impetigo.

2 In 5 of the 48 patients (or 10.4 per cent) who were treated with the ointment contact dermatitis developed.

3 By means of patch tests, 2 of these patients were proved to be sensitive to penicillin sodium. In our opinion the other 3 were undoubtedly sensitive to penicillin sodium, but we were unable to prove this by patch tests.

<sup>13</sup> Silvers, S. H. Contact Dermatitis from Amorphous Sodium Penicillin, *Arch. Dermat. & Syph.* 50:328 (Nov.) 1944.

## ACNE INDURATA IN IDENTICAL TWINS TREATED BY PENICILLIN

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**T**HE *Quarterly Cumulative Index Medicus* contains references to many articles on diseases occurring simultaneously in identical twins. However, there are almost no articles concerning diseases of the skin in such persons, and none whatever concerning acne.

The literature contains a few articles dealing with the treatment of acne with penicillin<sup>1</sup>. In general, it has been found that the drug has been of little value against this disease, although it must be noted that the doses were relatively small and the treatment was continued for only a short time. With these facts in mind, it seems worth while to report the use of penicillin in treating a pair of identical twins for acne indurata with accompanying subcutaneous abscesses.

Jack and Gene H. were first seen by me in November 1944. There were seven other children in the family, one of whom, a younger girl, had mild acne. The twins were born in May 1927, and as children they suffered at the same time from chickenpox, whooping cough and measles. Their acne began in the same month of 1941. It is of interest that these boys had always been inseparable, they had even insisted on sleeping together.

The 2 boys had been under the charge of another dermatologist for practically two years. They had received the usual treatments for acne, with little improvement, roentgen and ultraviolet irradiation, diet, various lotions and plenty of vitamins had accomplished practically nothing.

Physical examination showed that the boys were of almost the same height and that each weighed  $131\frac{1}{4}$  pounds (59.5 Kg). Their muscular development was poor. Each had the usual pustular acne of face, neck, torso, arms and upper part of the thighs, in addition, there were scattered lesions of acne indurata, chiefly on the face and neck. Both showed subcutaneous abscesses, some of which had coalesced into lesions of as much as 4 inches (10 cm) in diameter on the body and limbs. There was little acne on Jack's chest except at the edges of a practically solid mass of scar tissue.

Both boys were given the usual acne diet, solution of potassium arsenite U. S. P., wet dressings of magnesium sulfate, a solution of salicylic acid in alcohol and acetone, 5 per cent sulfathiazole in vanishing cream, ultraviolet radiation from a cold

1 Cohen, T. M., and Pfaff, R. O. Penicillin in Dermatologic Therapy, *Arch Dermat & Syph* **51** 172 (March) 1945. Franks, A. G., Dobes, W. L., and Romano, D. Penicillin in the Treatment of Cutaneous Disease, *ibid* **52** 14 (July) 1945. Morginson, W. J. The Clinical Use of Penicillin in Dermatology, *South M J* **38** 320 (May) 1945.

quartz mercury vapor lamp, and the opening and draining of pustules and abscesses. In cultures from the abscesses of both boys was a heavy growth of *Staphylococcus albus*. By the middle of March both boys were slightly improved.

On March 25, through arrangement with Dr. C. J. Van Slyke, of the United States Public Health Service, I received a 20 cc vial of penicillin in yellow wax, U. S. P. and peanut oil. On March 26, I began to treat Gene with this preparation as an ambulatory patient, he received 100,000 units in the morning and 200,000 in the late afternoon. On April 3 my supply of this preparation had run out and no more was obtainable. The improvement had been so great that it was decided to continue treatment for four days more with 100,000 units in water three times a day.

On April 20 practically all abscesses had disappeared and there were only two or three lesions of indurated acne remaining, but about half of the superficial acne still remained on both the face and the back. Gene had gained weight, his appetite was much better, and there was a decided change in his mental attitude.

On April 9 Jack entered the Suburban Hospital, where he remained through April 19, receiving 50,000 units of penicillin every three hours, a total of 300,000 units a day. On April 20 it was noted that there was great improvement but that on the site of several of the old abscesses small granulomas had developed. He was given an ointment for these consisting of 100,000 units of penicillin in 1 ounce (30 Gm) of hydrous wool fat and white petrolatum base, with directions to use it once a day after a bath. The result was gratifying, and by April 25 the granulomas had practically disappeared.

On September 17 both boys were seen. Each had gained weight, Gene weighed 134 pounds (60.8 Kg), and Jack weighed 133¼ pounds (60.4 Kg), neither had any deep abscesses or granulomas, but both showed one or two lesions of acne indurata on the face and neck and mild acne on the trunk. In addition, Jack had a few acne lesions on his forearms.

In conclusion, it may be said that these identical twins were cured of chronic subcutaneous abscesses associated with acne indurata, that the acne indurata had been greatly improved, and that the underlying acne had been somewhat helped. There was no essential difference in the results obtained with penicillin dissolved in yellow wax and peanut oil and those obtained with penicillin dissolved in water.

# PENICILLIN IN TOPICAL TREATMENT OF PYOGENIC INFECTIONS OF THE SKIN

Clinical and Laboratory Observations

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**T**HIS study was designed to correlate the clinical results of topical penicillin therapy for a group of superficial infections of the skin, with the sensitivity to penicillin in vitro of the organisms isolated. The widespread topical use of penicillin makes such a study desirable. Because penicillin is relatively nonirritating to the skin and non-sensitizing and because of its dramatically prompt action in favorable cases, the drug is admirably suited for the topical treatment of superficial pyogenic infections. Penicillin incorporated into ointment base is sufficiently stable if properly stored. Indeed, the rate of deterioration of the ointment is such that it may even be kept at room temperature for several weeks without serious reduction of activity.<sup>1</sup> Better knowledge of its stability permits extending the use of penicillin for topical application among patients whose access to refrigeration facilities is limited.

Our investigation was undertaken at the suggestion of the Air Surgeon's Office, Headquarters, Army Air Forces, to demonstrate why certain pyodermas respond promptly to application of the antibiotic and others do not. We present results in 45 cases of varied pyodermas studied clinically and bacteriologically at an Army Air Forces hospital in Florida. This is only a fraction of the patients with dermatologic diseases that we have treated with penicillin. The material is classified by diagnosis in tables 1, 2 and 3. On culture the majority of lesions yielded either beta hemolytic *Streptococcus* (Lancefield group A, C or G) or hemolytic *Staphylococcus aureus*, or both. Nonhemolytic *Staph aureus* was isolated in 2 cases. Anaerobic as well as aerobic conditions of cultivation were utilized. All strains of staphylococci isolated were found to be positive for the presumptive pathogenicity tests of production of coagulase and fermentation of mannitol. In addition to the organisms

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1 Gots, J. S., and Glazer, A. M. Stability and Activity of Penicillin in Solution and in Ointment, *War Med* 7:168 (March) 1945

named, diphtheroids, *Neisseria* and other bacteria were cultivated. These were recognized as obvious bacteriologic vagrants and were not studied further.

#### PROCEDURE AND METHOD

The management of each case conformed to the following procedure. After the initial dermatologic examination the patient was referred to the laboratory for bacterial cultures. Treatment with penicillin ointment was then carried out, three or four times during the day, either in the hospital or on an outpatient status. No other drugs were used to supplement the applications of penicillin, and within forty-eight to seventy-two hours it was possible to appraise the results of therapy. We found that when no distinct improvement could be detected in three days none would probably be forthcoming with additional treatment. Excluding several persons with impetigo which healed rapidly, each patient was treated continuously for one to three weeks.

With few exceptions it was demonstrated that the staphylococci recovered from lesions resistant to treatment were resistant to penicillin from the start. Beta hemolytic streptococci literally undergo dissolution overnight after treatment with penicillin. These organisms do not as a rule assume characteristics of acquired resistance, and the eruptions which they produce usually clear up with amazing rapidity.

Penicillin sensitivity of the organisms was determined by a tube dilution turbidity method, employing the glucose-yeast extract broth described by Schmidt and Moyer.<sup>2</sup> The inoculum consisted of a twenty-four hour broth culture ( $2$  to  $8 \times 10^8$  organisms per cubic centimeter) diluted 1:100 in the broth medium. This served as the diluent for preparing the final penicillin concentrations of 5, 1, 0.5, 0.32, 0.16, 0.08, 0.05, 0.04, 0.02, 0.01 and 0.005 units per cubic centimeter. After twenty-four hours of incubation at 37 C, the tubes were examined for growth, macroscopic turbidity being used as the index. The end point recorded was that tube containing the least concentration of penicillin which completely inhibited the growth of the organisms. By this method, *Staphylococcus aureus* strain H (a standard sensitive strain used for assay purposes) was completely inhibited by 0.04 unit per cubic centimeter. Organisms which grew in 5 units per cubic centimeter were considered resistant. In cases in which these organisms were carried to higher concentrations, 100 to 500 units per cubic centimeter was still insufficient for inhibition.

Various concentrations of penicillin, from 166 units<sup>3</sup> to 1,600 units<sup>4</sup> or more per gram of base, have been prepared in ointments by different authors. The optimal concentration probably lies in the lower levels of this range. With Garrod,<sup>5</sup> we doubt that there is any great advantage in

2 Schmidt, W. H., and Moyer, A. J. Penicillin. I. Methods of Assay, *J. Bact.* **47** 199 (Feb.) 1944.

3 Johnson, H. M. Penicillin Ointment for Pyodermas, *Arch. Dermat. & Syph.* **51** 270 (April) 1945.

4 Cohen, T. M. and Pfaff, R. O. Penicillin in Dermatologic Therapy. Report of Results in One Hundred Cases. *Arch. Dermat. & Syph.* **51** 172 (March) 1945.

5 Garrod, L. P. Action of Penicillin on Bacteria, *Brit. M. J.* **1** 107 (Jan. 27) 1945.

highly concentrated preparations for routine use. The ointment we employed contained approximately 800 units of penicillin per gram. We have tried various ointment bases: emulsion-type base, petrolatum, petrolatum with hydrous wool fat, cholesterol-petrolatum mixture and petrolatum with liquid petrolatum—incorporating 100,000 units of the drug in 120 Gm. of the vehicle.<sup>6</sup> We are not convinced that one base is materially superior in therapeutic effectiveness to another with equivalent concentration of penicillin. However, mention must be made of the *in vitro* tests performed by Templeton and his associates,<sup>7</sup> which suggested increased penicillin activity with increased water content of the ointment. Our emulsion type base was abandoned after a few instances of contact dermatitis were encountered. At the present time we employ a base of simple petrolatum. Contact sensitivity to penicillin was not observed among the cases reported herein.

#### CLINICAL MATERIAL AND RESULTS

The group "infectious dermatitis" (table 1) was designated to include cases of true infectious eczematoid dermatitis (Engman), of secondarily infected eczematoid dermatoses (contact dermatitis, dermatophytosis or dermatophytid with predominating pyogenic features) of external otitis and of dermatitis repens. Significant is the demonstration of a high incidence of penicillin-resistant strains among the staphylococci isolated (six sensitive and seventeen resistant strains), and a correspondingly poor therapeutic response to topical applications of penicillin. The role of epiphenomena, such as allergic bacterial sensitization and "eczematization," to account for the resistance to therapy of many of these cases, cannot be analyzed because it was impossible at any time to eliminate the pathogenic bacteria from the diseased skin.

In contrast to the foregoing the cases of impetigo and ecthyma (table 2) exhibited a reversed incidence of penicillin resistance (10 sensitive, 2 resistant strains of staphylococci), and the results of treatment with penicillin were excellent in the majority of cases. Our experience in treating impetigo in many other cases, not included in this series, justifies enthusiasm for the effectiveness of locally applied penicillin. It will be observed that among the cases listed are 2 of infections with sensitive strains of staphylococci which failed to yield to treatment with penicillin. Ammoniated mercury ointment in 1 case and sulfathiazole ointment in the other produced prompt cures.

6 Since this study was made, we have reduced the concentration of penicillin to 300 units per gram of ointment, with no observable loss of efficacy.

7 Templeton, H. J., Clifton, C. E., and Seeberg, V. P. Local Application of Penicillin for Pyogenic Dermatoses, *Arch. Dermat. & Syph.* **51**: 205 (March) 1945.

A reassay of sensitivity to penicillin, to determine if fastness may have supervened, was unfortunately not performed

The group "folliculitis" (table 3) included cases of involvement of the beard, neck and legs Staphylococci exclusively were isolated

TABLE 1—*Infectious Dermatitis Summary of Bacteriologic and Therapeutic Results*

Case No	Diagnosis	Location	Duration	Culture *	Penicillin Inhibition (Units/Cc)		Therapeutic Result †
					Staph	Strep	
1	Infectious eczematoid dermatitis	Left foot	7 yr	HSA, BHS	>500		P
2	Infectious eczematoid dermatitis	Feet, legs, hands	7 mo	HSA, BHS	>5	0.005	P
3	Infectious eczematoid dermatitis	Right foot	2 wk	HSA, BHS	0.5	0.005	P†
4	Infectious eczematoid dermatitis	Toes	10 days	HSA, BHS	>5	0.005	P
5	Infectious eczematoid dermatitis	Left palm, right sole	2½ yr	HSA, BHS	0.01	0.0025	G
6	Infectious eczematoid dermatitis	Toes	5 days	BHS		0.005	G
7	Infectious eczematoid dermatitis	Left leg	1 yr	HSA	>5		P
8	Infectious eczematoid dermatitis	Feet	10 mo	HSA	>5		P
9	Infectious eczematoid dermatitis	Left foot	2 mo	HSA	>5		P
10	Infectious eczematoid dermatitis	Feet	1 mo	HSA, BHS	>5		P
11	Infectious eczematoid dermatitis	Right axilla	5 days	HSA	>5		P
12	Infectious eczematoid dermatitis	Left ankle	2 mo	HSA, BHS	>5		F
13	Infectious eczematoid dermatitis	Forearm, right hand	2 yr	HSA	>5		P
14	Infectious eczematoid dermatitis, folliculitis	Ears, feet, chin	18 mo	NHSA	>5		P
15	Dermatophytosis, pyoderma	Toes	1 wk	HSA, BHS	>5	0.005	F
16	Dermatophytosis, pyoderma	Toes	3 wk	BHS		0.005	G
17	Dermatophytosis, pyoderma	Right foot	6 mo	HSA	5		F
18	Dermatophytosis, pyoderma	Toes	1 mo	HSA, BHS	>5	0.005	F
19	Dermatophytosis, pyoderma	Left foot	2½ yr	HSA, BHS	>5		P
20	Otitis externa	Ears	9 mo	HSA	>5		P
21	Otitis externa	Ears	2 yr	NHSA	0.05		G
22	Otitis externa	Ears	1 yr	HSA	0.04		G
23	Contact dermatitis, pyoderma	Scalp, face	5 days	HSA	5		G
24	Dermatitis repens	Right heel	5 mo	HSA, BHS	>500	0.005	P
25	Dermatitis repens	Hands	2 yr	HSA, BHS	>5	0.01	P

\* HSA = hemolytic Staphylococcus aureus, BHS = beta hemolytic streptococcus NHSA = nonhemolytic Staph aureus

† G = good result, cure complete or nearly complete F = fair result, partial improvement or relapse, P = poor result, treatment ineffective

‡ Sensitivity to emulsion type ointment base

sensitive to penicillin in 4 and resistant in 3 Results of treatment in these cases were only fair Our experience with a variety of these dermatoses especially of folliculitis (sycosis) barbae, indicates that although rapid healing often takes place there is a decided tendency

toward recurrence. Other authors have also encountered the problem of frequent reinfection.<sup>8</sup>

Patients with acne vulgaris were not treated. Bacteria isolated from abscesses and pustules in a number of cases of severe acne which we have observed usually consisted of nonpathogenic staphylococci or penicillin-resistant staphylococci. In general, penicillin therapy for acne

TABLE 2—*Impetigo and Ecthyma Summary of Bacteriologic and Therapeutic Results*

Case No	Diagnosis	Location	Duration	Culture *	Penicillin Inhibition (Units/Ce)		Therapeutic Result †
					Staph	Strep	
26	Impetigo	Face	4 days	HSA	0.04		G
27	Impetigo	Knee, face	1 wk	BHS		0.005	G
28	Impetigo	Face, trunk	2 wk	HSA	0.05		G
29	Impetigo	Face, penis	10 days	HSA, BHS	0.04	0.005	G
30	Impetigo	Face	1 wk	HSA	0.05		P
31	Impetigo	Face, trunk	3 wk	HSA, BHS	>5		P
32	Impetigo	Face	1 wk	HSA	0.05		G
33	Impetigo	Abdomen	5 days	HSA	0.04		G
34	Impetigo	Scalp, face	2 wk	HSA, BHS	0.04		G
35	Ecthyma	Legs	18 mo	HSA, BHS	>5		P
36	Ecthyma	Feet	4 wk	HSA, BHS	0.05	0.01	P
37	Ecthyma	Right leg	10 days	HSA	0.02		G
38	Impetigo, folliculitis	Face	2 mo	HSA	0.05		G

\* HSA = hemolytic *Staphylococcus aureus*, BHS = beta hemolytic streptococcus

† G = good result, cure complete or nearly complete. F = fair result, partial improvement or relapse, P = poor result, treatment ineffective

TABLE 3—*Folliculitis Summary of Bacteriologic and Therapeutic Results*

Case No	Diagnosis	Location	Duration	Culture *	Penicillin Inhibition (Units/Ce)		Therapeutic Result †
					Staph	Strep	
39	Folliculitis	Beard	2 wk	HSA	0.04		G
40	Folliculitis	Beard, neck	20 mo	HSA	0.02		G
41	Folliculitis	Beard	2 yr	HSA	>5		P
42	Folliculitis	Legs, face	18 mo	HSA	>5		P
43	Folliculitis	Beard	1 yr	HSA	0.05		G
44	Folliculitis	Beard	11 wk	HSA	>5		P
45	Acne necrotica	Scalp, forehead	6 yr	HSA	0.04		F

\* HSA = hemolytic *Staphylococcus aureus*

† G = good result, cure complete or nearly complete. F = fair result, partial improvement or relapse, P = poor result, treatment ineffective

is hardly logical. The unfavorable results observed by others<sup>9</sup> confirm this conclusion. On the other hand, staphylococci from furuncles are found usually to be sensitive to penicillin.

8 (a) Taylor, P. H., and Hughes, K. E. A. Infective Dermatoses Treated with Penicillin, *Lancet* 2:780 (Dec 16) 1944. (b) Roeburgh, I. A., Christie, R. V., and Roeburgh, A. C. Penicillin in Treatment of Certain Diseases of the Skin, *Brit. M. J.* 1:524 (April 15) 1944.

9 Garrod.<sup>5</sup> Roeburgh, Christie and Roeburgh.<sup>8b</sup>



## COMMENT

Data concerning the use of penicillin for the treatment of cutaneous infections caused by staphylococci indicate that the antibiotic, while eminently satisfactory in many cases, is far from universally effective. This study of an unselected series of cases of pyogenic dermatoses with regard to the bacteriologic observations and the degree of sensitivity to penicillin of the isolated organisms, particularly the staphylococci, provides an explanation for the sometimes erratic results encountered in topical therapy with penicillin. Approximately half of the patients infected with staphylococci alone or in conjunction with streptococci harbored penicillin-resistant strains (in 22 of 42 cases). A few patients exhibited initial improvement with applications of penicillin ointment, then their dermatoses remained at a stationary level or relapsed, a circumstance undoubtedly due to elimination of the streptococcus moiety of a combined infection, leaving the penicillin-resistant staphylococcus unaffected. (So far not one instance of resistance or fastness to penicillin has been encountered among the strains of beta hemolytic streptococci isolated, and we regard determination of the sensitivity to penicillin of these streptococci as an unnecessary routine procedure.) Moreover, we observed that when the resistance of a strain of staphylococci was of such degree that growth was not inhibited by 5 units of penicillin per cubic centimeter in vitro the strain would not respond to treatment with penicillin ointment containing 800 units in each gram. Certainly an infection with an organism so resistant will never respond to intramuscular injections of penicillin, by which average maximum blood levels of about 0.6 unit per cubic centimeter are generally attained. For purposes of expediency, therefore we consider it unnecessary to carry testing of sensitivity to penicillin beyond the concentration of 5 units per cubic centimeter. It will be observed in table 1 that in 2 of our cases staphylococci not inhibited by 500 units of penicillin per cubic centimeter were isolated and probably there were many more strains of highly resistant staphylococci in this series. Resistance of staphylococci to as high as 10,000 units of penicillin per cubic centimeter has been recorded<sup>10</sup>.

The question may be asked: Is it advisable in cases of pyoderma in which local treatment with penicillin is contemplated to perform routinely sensitivity studies on the bacteria? This can be answered in the negative. With penicillin ointment now readily available and relatively inexpensive a therapeutic test, as we have shown, will yield practically the same information qualitatively as the sensitivity test. We have accumulated evidence that treating pyodermas with penicillin ointment may in some

10 Keyes J. E. L. Penicillin in Ophthalmology. I. A. M. A 126:610 (Nov. 4) 1944.

cases increase the degree of resistance of staphylococci to penicillin, thereby accounting for infectious relapse and failure of treatment. Fortunately, this is not of common occurrence. Taylor and Hughes<sup>8a</sup> reported that after treatment with an ointment containing 200 units of penicillin per gram certain sensitive strains of staphylococci from cutaneous infections became fast. They attributed the accident to poor diffusibility of penicillin from the ointment base and to deterioration. The difficulty did not arise with ointment containing 400 units of penicillin per gram. On the other hand, among a series of cases of infected wounds and abscesses treated with penicillin intramuscularly or intravenously, Gallardo<sup>11</sup> found that 9.4 per cent of coagulase-positive strains of staphylococci acquired fastness to penicillin during the course of treatment, in addition to 12.9 per cent of naturally resistant strains among the pathogenic staphylococci. Observations made by Crawford and King<sup>12</sup> among a group of infections of the eyes and lid margins indicated that when bacteriologic relapse occurred the responsible organisms were no less sensitive to penicillin than were the original invaders.

The importance of bacteriologic examination of the skin in augmenting the understanding of the pyodermas deserves great emphasis. Cultural investigations, we suggest, are especially valuable in studying chronic, treatment-resistant eczematoid eruptions. Clinical judgment and laboratory tests must be called on to decide whether the bacteria isolated are primary pathogens or secondary invaders of an underlying dermatosis and what treatment might be most effective under the circumstances. Claims for the efficacy of penicillin in topical dermatologic therapy therefore require thoroughgoing bacteriologic support. Lacking this, discrepancies of experience in treating pyodermas can be expected. It is possible that there are local differences in incidence of strains of staphylococci in various parts of the world, just as there are of hemolytic streptococci. Areas in which carriers of Lancefield group A streptococci abound are likely to show also an increased incidence of streptococcal contamination of the skin.<sup>13</sup> In subtropical Florida, staphylococci are found more frequently in pyodermas than are streptococci, but the material reported by Roxburgh<sup>5b</sup> from England gives bacteriologic observations almost identical with those in our own cases. There are no clinical features that distinguish pyodermas caused by penicillin-sensitive strains from those caused by penicillin-resistant strains.

11 Gallardo, E. Sensitivity of Bacteria from Infected Wounds to Penicillin. II. Results in One Hundred and Twelve Cases, *War Med* **7** 100 (Feb.) 1945.

12 Crawford, T., and King, E. F. The Value of Penicillin in the Treatment of Superficial Infections of the Eyes and Lid Margins, *Brit. J. Ophth.* **28** 373 (Aug.) 1944.

13 Hare, R. Haemolytic Streptococci in Normal People and Carriers, *Lancet* **1** 85 (Jan. 18) 1941.

An attempt to explain the predominance of penicillin-resistant staphylococci among the patients with infectious dermatitis (table 1) stimulates conjecture regarding the host-parasite relationships which determine the characteristics of an inflammatory reaction. Needless to say, none of the patients in this study had had previous treatment with penicillin, and thus any possibility of induced resistance (fastness) is precluded. Most of the infections were chronic and indolent, which suggested invasion by organisms of low grade virulence. When various pathogens are made resistant to penicillin, a great and apparently permanent decrease in virulence occurs<sup>14</sup>. Similar loss of virulence has been reported in organisms resistant to sulfonamide compounds<sup>15</sup>. Also the incidence of resistance to penicillin is higher among nonpathogenic strains of staphylococci than among pathogenic strains. The nature of the inflammatory response, then, is dependent on the virulence of the organism, which, in turn, is apparently associated with its resistance to penicillin.

When resistance to penicillin increases, there is a reduction of the rate of growth and of enzymic activities of the organism,<sup>16</sup> and when the growth of an organism is retarded the host-parasite balance will be disturbed. Hobby, Meyer and Chaffee<sup>17</sup> have shown that penicillin is effective only when active multiplication is taking place. When the rate of growth of staphylococci decreases, the organisms become less susceptible to the action of penicillin. If the enzymic activities are greatly reduced with increased resistance there is no a priori reason why other products elaborated during normal metabolism (hemotoxin, lethal toxin, dermonecrotic toxin, leukocidin, Duran-Reynolds spreading factor) should not also be affected.

Our analysis of clinical statistics reveals some distinct limitations of penicillin in the treatment of many staphylococcal infections. A number of valuable antibacterial drugs are available for topical treatment of penicillin-resistant infections of the skin: mercurials, sulfonamide compounds and chlorahydroxyquinoline, to name some common ones. A limited experience which we have had with tyrothricin for dermatologic infections suggests that it too is an effective antibacterial

14 McKee, C. M., and Houck, C. L. Induced Resistance to Penicillin of Cultures of Staphylococci, Pneumococci and Streptococci, *Proc Soc Exper Biol & Med* **53** 33 (May) 1943.

15 Horsfall, F. L., Jr. The Effect of Sulfonamides on Virulence of Pneumococci, *J Clin Investigation* **21** 647 (Sept) 1942.

16 Abraham, E. P., Cham, E., Fletcher, C. M., Florey, H. W., Gardner, A. D., Heatley, N. G., and Jennings, M. A. Further Observations on Penicillin. *Lancet* **2** 177 (Aug 16) 1941. McKee and Houck<sup>14</sup>.

17 Hobby, G. L., Meyer, K., and Chaffee, E. Observations on the Mechanism of the Action of Penicillin, *Proc Soc Exper Biol & Med* **50** 281 (June) 1942.

agent, in some respects superior to penicillin. Undoubtedly, more and more potent antibiotics or combinations of antibiotics will in time be developed, to the enhancement of dermatologic therapy.

#### SUMMARY AND CONCLUSIONS

The results of local treatment with penicillin ointment of pyogenic dermatoses are summarized as follows: (1) impetigo and ecthyma, results good, (2) folliculitis, results fair, (3) infectious dermatitis (including infectious eczematoid dermatitis, infected eczematoid dermatoses, dermatitis repens and external otitis), results poor.

The variation in results of treatment is accounted for by differences among strains of infecting staphylococci, as manifested by wide ranges of sensitivity to penicillin in vitro. A predominance of penicillin-sensitive staphylococci are isolated from lesions of impetigo, as contrasted with a predominance of penicillin-resistant staphylococci from the eczematoid lesions of infectious dermatitides. Resistant strains of beta hemolytic streptococci have not been encountered. The therapeutic results with penicillin topically parallel closely the degree of sensitivity to penicillin of the micro-organisms as determined in vitro.

Technical Sergeant Joseph L. Sardinas, Medical Department, Army of the United States, assisted in the laboratory procedures and Technical Sergeant Richard H. Swame, Medical Department, Army of the United States, prepared the ointments.

## TOKELAU IN GUATEMALA

JULIO E GOMEZ Ch, MD

GUATEMALA

THE FIRST description of *tinea imbricata*, or tokelau, dates from the year 1686 when William Dampier,<sup>1</sup> in a record of his voyages, referred to a scaling cutaneous disease encountered in the Philippines, Mindanao, the Marianas and Guam. It was subsequently observed in the islands of the Pacific by Entrecasteux (1780),<sup>2</sup> Alibert (1832),<sup>3</sup> Meederwoort (1839),<sup>4</sup> Fox (1844)<sup>5</sup> and Turner (1869).<sup>6</sup> The disease was not known in the Tokelau Islands until 1869, when it was introduced from the Gilberts.

In 1874 Tilbury Fox<sup>7</sup> demonstrated fungi in the squames, and the observation was confirmed in 1878 by Koniger.<sup>8</sup> Manson (1879)<sup>9</sup> differentiated tokelau from herpes circinatus. Sabouraud<sup>10</sup> asserted that it was caused by *Trichophyton*. Many of the early attempts to culture the fungus failed, however, and led to the erroneous conclusion that it was a species of *Aspergillus*.

Tokelau was probably introduced into America in pre-Columbian times by immigrants from the Orient. Paranhos and Leme<sup>11</sup> observed a case in Brazil in 1904 and Mora Mora<sup>12</sup> reported a case (without

From the Universidad de San Carlos de Guatemala

1 Dampier, W. Voyage autour du monde, Paris, 1789

2 Entrecasteux, cited by Manson<sup>9</sup>

3 Alibert, J. L. M. A. Precis theorique et pratique sur les maladies de la peau, ed. 2, Paris, Caille et Ravier, 1832

4 Meederwoort, cited by Manson<sup>9</sup>

5 Fox, J. L. Narrative of the United States Exploring Expedition During the Years 1839, 1840, 1841, 1842 by Charles Wilkes, Philadelphia, Lea & Blanchard, 1845, vol. 5, pp. 40-41 and 104-105

6 Turner, G. A. Notes of Practice in Samoa, Glasgow M. J. 2:502 (Aug.) 1870

7 Fox, T. On Tokelau Ringworm and Its Fungus, Practitioner 2:304, 1874

8 Koniger. Ueber den polynesischen Ringwurm auf den Carolinen-, Gilbert- und Samoa-Inseln, Virchows Arch. f. path. Anat. 72:403, 1878

9 Manson, P. Notes on *Tinea Imbricata*, an Undescribed Species of Body Ringworm China Imp. Customs M. Rep. (1878) 16:1, 1879, M. Times & Gaz. 2:342, 1879

10 Sabouraud, cited by Figueroa and Conant<sup>14</sup>

11 Paranhos, U. *Tinea Imbricata* in Brazil. J. Trop. Med. 7:153, 1904  
Paranhos, U. and Leme, C. P. Note on the *Tinea Imbricata* in Brazil, *ibid.* 9:129, 1906  
Leme, C. P. Contribuição ao estudo do tokelau, Rio de Janeiro, 1903

12 Mora Mora, cited by Figueroa and Conant<sup>14</sup>

mycologic study) in Colombia in 1935. Two cases were reported in El Salvador in 1937 and 1938. In Guatemala Dr. Francisco Diaz A,<sup>13</sup> in 1937, presented a case before the Primer Congreso Sanitario Centro-Americano. That patient was examined in connection with the present study. A second Guatemalan case, with mycologic study, was reported by Figueroa and Conant.<sup>14</sup> Dr. Diaz, in a sanitary survey of Guatemala, has observed this mycosis in the states of Solola, Chimaltenango, Suchitepequez and Huehuetenango.

The disease is known under many different names, among which are *tinea imbricata*, *pita*, *buckwai*, *oune*, *Kune-Kune*, *tukune-kune*, *gune*, *gogo*, *gugo*, *gugomon*, *cascado gorap*, *koerab*, *korab-besi*, *loesoeng*, *lusung*, *lofa-tokelau*, *etemané*, *talofat*, *kilinaí*, *dermatosis chronica figurativa exfoliativa* of Thomson, *herpes desquamans* of Turner, *dermatomycosis koerab*, *tropical ichthyosis*, *herpes* of Manson, *sarna de Dajak* and (in Guatemala) *jote*.

The fungus, *Trichophyton concentricum* R. Blanchard 1895, also has a number of synonyms: *Lepidophyton concentricum*, *Aspergillus lepidophyton*, *Aspergillus tokelau*, *Endodermophyton concentricum*, *E. indicum* and *E. tropicalis*.

Tokelau is a contagious, inoculable, pruriginous, erythematous-squamous dermatophytosis in which the scales form an annular concentric pattern which becomes modified by the confluence of the spreading rings. The infection is chronic (duration of sixty-four years in one of the cases in this series), it may involve the entire cutaneous surface, and it is resistant to treatment.

Lesions may develop from ten to twelve days after inoculation with infected scales and from fifteen to eighteen days after inoculation with a pure culture. They begin as small round vesicles which are replaced by reddish macules. The fungus penetrates the epidermis to the malpighian layer, where it grows readily, separating the stratum granulosum from the stratum corneum. Separation of these layers produces the characteristic scale, and peripheral growth of the lesion and repetition of the process in the older portions of the lesion result in the peculiar pattern of this dermatophytosis. There is pruritus, which is increased by certain foods, heat, salt water and exposure to the sun. Although any cutaneous surface may be involved, in the cases included in this series lesions were most prominent on the trunk.

The scale which is characteristic of tokelau is at first small, thin, dirty white or yellowish white. As it becomes thicker and larger it

13 Diaz A, F, in Primer congreso sanitario de Centro America y Panama, Guatemala, Impreso en la Tipografia Nacional, 1937.

14 Figueroa, H, and Conant, N. F. First Case of Tinea Imbricata Caused by *Trichophyton Concentricum* Blanchard 1896, Reported from Guatemala, Am J Trop Med 20: 287, 1940.

retains the same color. The most striking characteristic of this mycosis is the regular pattern of concentric arcs of circles. This pattern is formed by the scales, which become detached at the inner edge while the outer edge remains attached. As the diameter of the ring of scales increases by peripheral growth new rings form successively within the first, often at such frequent intervals that the scales of the outer ring may overlap those of the second as the tiles on a roof. Each successive ring can be felt as a ridge if a finger is rubbed radially across the lesion. Autoinoculation by scratching initiates new lesions, and the coalescence of these forms the pattern by which a recent infection is easily recognized. In an infection of long duration this pattern may disappear and large areas of skin may present only an irregular scaling. The

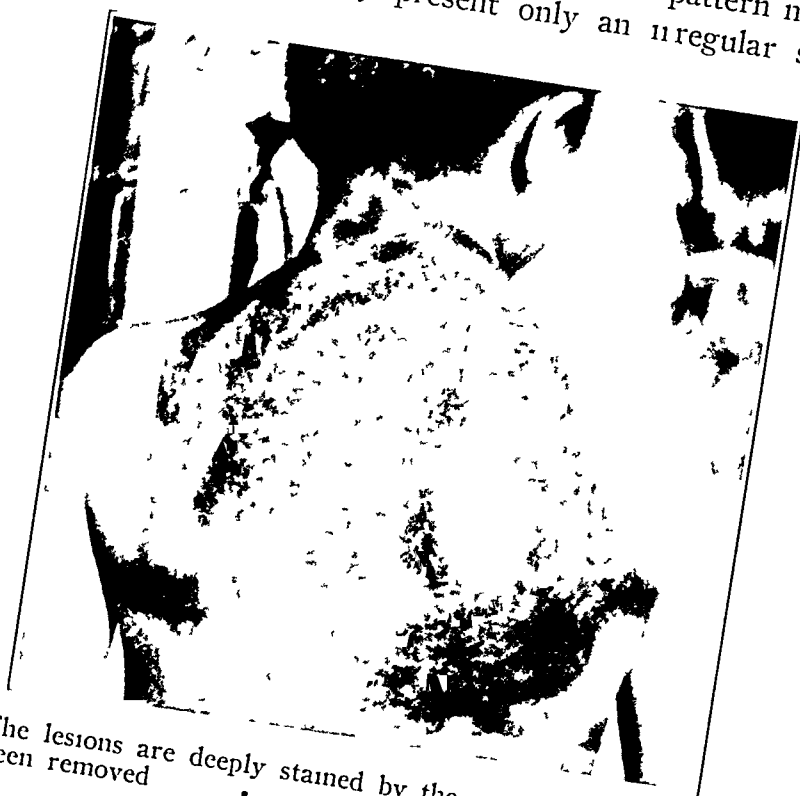


Fig. 1—The lesions are deeply stained by the method described, and the free scales have been removed.

scales may be attached to neighboring scales to form bands separated by dark-colored skin. On the hands the scales may be thick, large and yellowish and may be separated by furrows which are red but do not ooze serum. The skin of the plantar surfaces of the foot was exceptionally thick in the patients examined in this study. There may be longitudinal grooves in the nails, which are thickened and of ash gray color, with a raised border. The skin is abnormally dry except in the presence of eczematoid lesions. In the latter case there is regional adenopathy.

Besides the classic type of tokelau four variations were observed in this series: a diffuse type in which the annular pattern is not evident,

the East Indian type in which scales are widely separated by normal skin, a desquamative type with early shedding of the scales and a mixture of the three types

The disease must be differentiated from ichthyosis, dermatitis exfoliativa, mal del pinto, favus, syphilis, pityriasis rubia grave of Hebra-Jadassohn and other types of dermatophytosis

Tokelau is most common near the coast in the warm humid climate of tropical countries, but in Guatemala it appears to be more frequent in a region located from 80 to 170 kilometers from the Pacific Coast at an altitude of 3,000 to 5 000 feet (900 to 1 500 meters) It rarely develops in children younger than 10 years of age In Guatemala it is more common in women than in men and is seen in rural peasants



Fig 2—Lesions on the upper part of the chest and abdomen stained by the gentian violet method described The duration of the lesions was six years

Predisposing factors appear to be poor personal hygiene and deficient diet

The patients with tokelau studied in this investigation were all workers in the Finca Santo Tomas P in the state of Solala This finca is on the northwest slope of the volcano Atitlan 93 kilometers from the Pacific Ocean The altitude is 4,200 feet (1,260 meters), the average temperature is 19 C (66.2 F), the annual rainfall is high, and the humidity is above 85 per cent The population of the finca numbers 210, and tokelau was observed in 11, of whom 8 were women All those infected were native laborers who live in crowded small, thatched houses Although they live in close proximity to domestic animals the mycosis was not observed in the latter The diet consists of beans, rice,



tortillas and coffee, with rare additions of meat and bread. The potable water has a low iodine content (goiter zone).

In order to facilitate photography of the lesions they were prepared by a method recommended by Dr. Horacio Figueroa. The lesions were rubbed vigorously with a compress saturated with 10 per cent gentian violet. On the following day the patient was instructed to bathe, taking care not to rub off the scales. The scales retain the stain while the intervening skin is decolorized.

In the isolation of the fungus the lesions were cleansed by rubbing for two minutes with a 60 per cent solution of alcohol. After the lesion was dry the scales were scraped with a sterile, dull scalpel into a sterile labeled test tube. For microscopic examination the scales were placed with the lower side up on a microscope slide in a drop of 40 per cent

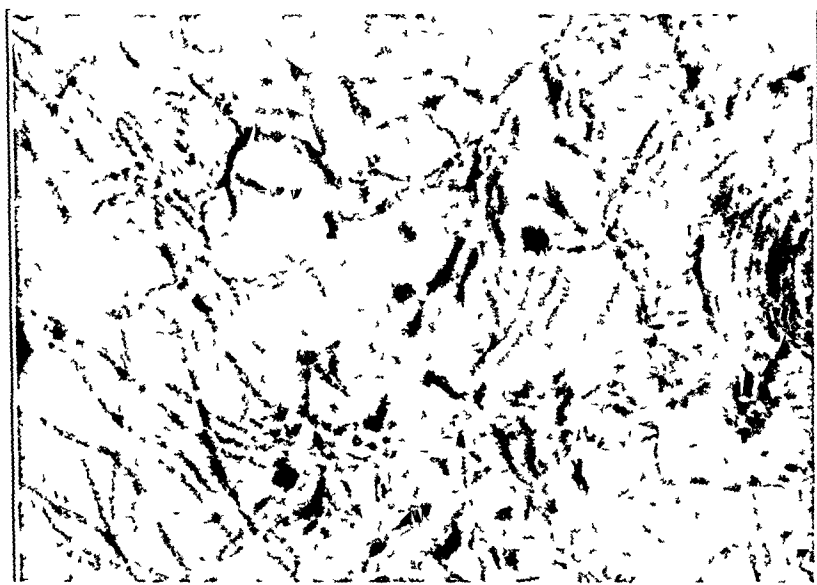


Fig. 3—Appearance of the hyphae in scales

solution of potassium hydroxide (a 10 per cent solution is equally effective) or in lactophenol and covered with a cover slip. Scales were also treated for forty-eight hours with the clearing medium of Oliveira Castro, which has the following composition: 60 cc each of absolute ethyl alcohol and distilled water, and 240 cc of chemically pure phenol crystals. Add 1 sq. cm. of Kodak carmine paper to each of 10 cc. of the clearing fluid.

In the scales septate hyphae of the fungus are numerous, branching freely and running in all directions to form an easily demonstrated mycelium (fig. 3). They are of fairly uniform diameter, except that in older hyphae where there are many septums the individual cells may be slightly enlarged, imparting a beaded appearance. There are also occasional large cells from which hyphal branches radiate.

The fungus was isolated in culture on Sabouraud's agar (glucose 20 Gm , peptone 10 Gm , distilled water 1,000 cc , agar 18 Gm ) by the following method Scales were placed in an 80 per cent solution of alcohol for fifteen minutes, dried between two sterile slides and planted on agar slants The fungus grows slowly, at first forming a small, heaped-up, irregular colony As the colony increases in size radial folds and furrows develop from the center and some colonies become cerebriform There is a flat, thin peripheral zone in older colonies The surface is covered with a short white mycelium, giving the colony a gray color

In 7 of the cases studies of the blood were made These showed in all cases a negative Wassermann reaction and an eosinophilia varying from 12 to 17.6 per cent Examinations of the stools of 9 of the patients revealed one or more of the intestinal parasites *Uncinaria* *Ascaris* and *Trichocephalus* It was not determined whether the eosinophilia was due to the mycosis or to the parasites

Tokelau does not respond well to treatment The recommended procedures were used in these cases without complete success Because of its efficacy in other mycoses iodine was tested One preparation, iodoxy-quinolinsulfonate of sodium, showed considerable promise and merits further trial

#### SUMMARY

Eleven cases of tokelau occurring in the indigenous population of one finca in Guatemala were studied in detail The mycosis appeared in classic form Treatment has been only partially successful

## PEMPHIGUS VULGARIS

Successful Results Following Transfusion with Blood from Persons Who Had  
Recovered from the Disease

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AND

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**P**EMPHIGUS vulgaris is a constitutional disease whose most obvious and diagnostic manifestations are in the skin, thus resembling the exanthems. In recent years the etiologic agent has been thought to be a virus, and reports have already been made<sup>1</sup> of the isolation of strains in 4 cases of the disease. The relation of the strains to pemphigus vulgaris had not been established when the reports appeared, but subsequent data, now in preparation for publication,<sup>2</sup> indicate that the RP strain of virus is the etiologic agent of the disease. It was accordingly felt that antibodies which would neutralize the virus would be present in the blood serum of persons who had recovered from the disease. Owing to the high mortality and relative rarity of occurrence of pemphigus vulgaris, such persons are few in number and difficult to find. In response to nation-wide appeals, however, 2 women were found whose blood was used for transfusions to 2 men seriously ill with pemphigus vulgaris.

In this paper are presented the case histories of the 2 women who had recovered from the disease and the 2 men who received blood from them.

### REPORT OF CASES

#### *A. Cases of persons recovered from pemphigus vulgaris*

CASE 1—S. J., a married gentle woman aged 27, was born in Pennsylvania of Polish parents. On Aug. 28, 1944 she felt more than usually tired, and on the following day she complained of discomfort around the eyes and mouth and also in the genital region, accompanied with the appearance of small vesicles on the conjunctivas and lips. When she awoke on the morning of August 30, there was considerable edema of the vulva and a generalized eruption which consisted

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1 Grace, A. W. and Suskind, F. H. An Agent, Transmissible to Mice, Obtained During a Study of Pemphigus Vulgaris, *Proc. Soc. Exper. Biol. & Med.* **37**: 324, 1937. An Investigation of the Etiology of Pemphigus Vulgaris, *J. Invest. Dermat.* **2**: 1, 1939.

2 Grace, A. W. The Etiologic Agent of Pemphigus Vulgaris, to be published.

of "red spots with little blisters in the center" By 10 p m, September 2, the oral temperature had risen to 104 F and there were erythematous, macular lesions—some of which had small vesicular centers—in the conjunctivas and nasal orifices, on the lingual and buccal mucosae and in the vulval and perianal areas The most distressing symptom was soreness in the mouth During the next two days, a further development was the appearance of large bullae on the arms, legs, trunk and chin, the temperature meanwhile remaining at 104 F On the morning of September 5, she was desperately ill and was seen by a dermatologist, Dr Harry Saunders, who made the diagnosis of pemphigus vulgaris The temperature began to fall on September 6, but an accurate measurement was not possible, owing to the extreme discomfort of the mouth and anus Next day the temperature was normal, but the cutaneous lesions were bleeding and malodorous and had to be covered with dressings until September 15 Two days later she was allowed to get out of bed, and she was discharged from the hospital on September 24, at which time the lesions of the mucous membrane had disappeared and the skin was normal except for slight scaling in several areas In a review of the internal and external medications employed in the treatment of the patient no substance was discovered which could be incriminated as the cause of the illness There was no relapse between the time of the patient's discharge from the hospital and the first visit for the purpose of this study, on June 21, 1945

CASE 2—D T, a married Jewish woman, was born in Minsk, Russia, in 1900 She became ill in New York city in 1921, a few hours after eating a meal of fried mushrooms The initial picture was that of an acute gastrointestinal upset with diarrhea, vomiting and cramps in the abdomen Two days later, when the gastrointestinal symptoms had subsided, the gums became covered with a "white film" which soon extended to involve the throat, tongue and mouth This was followed by ulceration of the involved areas, especially the tongue The disease smoldered in the mouth for the succeeding six months, during which time one area of the mucosa would heal and another would break down At the end of that time, without any change in the condition of the mouth, the lips and vulva became edematous Numerous exposures to ultraviolet rays were given as a therapeutic measure to the lips and vulva and had the effect, according to the patient, of spreading the disease to the boundaries of the irradiated skin, thus producing oozing, crusted, edematous, erythematous, confluent lesions on the circumoral areas and the upper inner portion of the thighs With the exception of denudation of the skin of the umbilicus, no other portion of the integument was involved At the height of her illness she was seen by Dr L D Bulkley, who made a diagnosis of pemphigus The disease persisted in the mouth for approximately one year and in the circumoral area for another six months, a total duration of illness of about eighteen months During that period there was little elevation of temperature, and the weight fell from 146 to 80 pounds (66.2 to 36.3 Kg) In a review of the internal and external medicaments employed in the treatment of the patient none was found which could be incriminated as the cause of the disease There was no relapse between the time of the subsidence of the cutaneous lesions, in 1922, and the first visit for the purpose of this study, on June 26, 1945

*B Cases of persons sick with pemphigus vulgaris who received transfusions of blood from persons who had recovered from the disease*

CASE 3—H W, a married Jewish man aged 54, was born in Poland He was admitted to the Long Island College Hospital on March 26, 1945, after an

illness of eighteen months' duration, which illness began with "sores" in the mouth and later showed, in addition, blisters and crusted lesions on the skin and on the perianal areas. At the time of admission, the mouth and tongue presented numerous areas from which the mucosa was denuded, causing considerable soreness of the mouth. Similar areas of shallow ulceration were present in the perianal area. Collapsed pea-sized bullae with surrounding erythematous zones were found on the arms, legs, back and abdomen. There was no elevation of temperature. Treatment with penicillin was commenced, 40,000 Oxford units being given intramuscularly every three hours for a total of 6,960,000 units. With each of two of the daily doses of penicillin 6 cc of human immune globulin (placental) was mixed and administered for a total of 216 cc. After this treatment had been given for nine days, the lesions began to dry and at the time of the patient's discharge from the hospital, on April 15, the skin was practically clear except for a small crusted area in the right inguinal region. The eruption in the mouth, however, was unchanged. For the next seven weeks H W resumed his business activities. He was hospitalized again on June 6, 1945, with lesions of the vegetating type in the inguinal and perianal areas. The general condition had deteriorated, and the temperature was 101 F. Treatment was resumed, with penicillin, immune globulin (placental) and Germanin, and during the period of treatment the involved areas in the mouth, the inguinal and the perianal regions increased in extent. Fresh crusted lesions appeared on the thighs, trunk, neck, chin and scalp, the temperature ranged between 101 and 102 F and the general condition continued to deteriorate. On June 21 and on June 27 he was given a transfusion of 500 cc of citrated blood, taken from S J and D T, respectively. There was no untoward reaction to the receipt of the blood, nor had any improvement occurred at the time of the second transfusion. On June 30, however, the temperature fell to normal, all the cutaneous lesions began to dry and recede until by July 4 they had disappeared, leaving sharply demarcated, dusky erythematous flat areas at their former sites. The lesions in the mouth also cleared up. On July 4, a cerebral accident produced right hemiplegia and loss of speech. The skin remained clear until July 26, when small clusters of pinhead to match-head sized pruritic vesicles appeared in the right inguinal region and on the right side of the scrotum. These clusters gradually extended, until, by August 24, palm-sized plaques of oozing granulation tissue were present on the upper inner aspect of both thighs and the scrotum and perianal area were involved with similar lesions. A transfusion of 500 cc of citrated blood from S J was given, following which the cutaneous lesions began slowly to recede until by October 1 they had disappeared, leaving a flat, dusky erythematous residuum as before.

CASE 4—H S, a married Jewish man aged 61, was born in New York city. He was admitted to the Long Island College Hospital on July 9, 1945, after an illness of six months' duration, which began with a cluster of vesicles in the left axilla and progressed with the formation of blisters and denuded areas on the limbs, trunk, mouth and perianal regions. At the time of his admission, the most striking lesion was a denuded, painful, oozing area 15 cm in diameter on the upper right portion of the chest. Macerated epithelium was present in the mouth and perianal regions, and crusted lesions, some with concomitant collapsed bullae, were to be seen on the back, abdomen, inguinal regions and soles. From the day of admission the general and cutaneous conditions deteriorated. New bullae, bacteriologically sterile on aerobic and anaerobic culture, appeared in fresh sites at frequent intervals without diminution in the activity of older lesions. More than 60 per cent of the skin surface presented large raw, painful areas, the face was slightly edematous, and the appetite was impaired. No medication was given.

until August 11 with the exception of sedation for pain and the application of boric acid ointment dressings on the cutaneous lesions to prevent them from sticking to the bed linen. On that date, when he was too weak to leave the bed, a transfusion was given of 500 cc of citrated blood taken from D. T. Within twelve hours the systemic condition began to improve, and at the end of forty-eight hours the cutaneous lesions were less erythematous and less painful and were receding. On the fourteenth day after the transfusion all of the cutaneous lesions had been epithelized, and their sites were marked by sharply delimited, dusky erythematous, flat areas. On September 10 two crusted lesions, each  $1\frac{1}{2}$  inches (3.8 cm) in diameter, appeared within the site of the large lesion which had been present on admission on the upper right portion of the chest. These new lesions persisted unchanged until October 10, at which time this report was compiled. At no time did the patient have any elevation of temperature.

#### COMMENT

It is impossible to escape the conclusion that the rapid disappearance of the systemic and cutaneous manifestations of both H. W. and H. S. was due to the blood transfusions which they received. Such blood, therefore, must be regarded as containing antibodies which neutralized, temporarily at least, the activity of the agent of pemphigus vulgaris. It is known that infections due to viruses may give rise to circulating neutralizing antibodies which can be demonstrated by protection tests for periods which, in the case of yellow fever, may be as long as sixty years after the acquisition of the disease. The relapses which occurred in both H. W. and H. S. can be regarded as being due to the low total amount of antibodies which they had received. When a sufficient number of persons who have recovered from pemphigus have been located, longer lasting therapeutic results will probably be achieved by transfusions of their blood at intervals of three or four weeks.

#### SUMMARY

The cutaneous and constitutional manifestations of pemphigus vulgaris in 2 persons seriously ill with the disease cleared rapidly after transfusion of blood from persons who had recovered from the disease.

# SPOROTRICHOSIS WITH RADIATE FORMATION IN TISSUE

Report of a Case

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**R**ADIATE formation on cells of *Sporotrichum* was first observed by Splendore in 1908 and termed by him asteroid formation<sup>1</sup> These star-shaped bodies were found extracellularly in pus obtained from a verrucous, vegetative, hard and somewhat elastic lesion, present for twenty days, on the right side of the face of an Italian woman living in São Paulo, Brazil<sup>2</sup> Pure cultures of the fungus were obtained from this lesion and from two lymph nodes, the size of kidney beans, just beneath the primary site The lesion began as a small button, increased in size gradually to take on the verrucous appearance and was a little pruritic The nodes developed secondarily The lesion cleared in a few days with potassium iodide taken internally and topical application of mild mercurous chloride ointment The cultures were identified as *Sporotrichum* and because of the radiate formation of the cells in tissue a new species was created, *Sporotrichum asteroides* Splendore, 1908 The cultures were sent to de Beurmann and Gougerot, who considered the fungus a variety of *Sporotrichum Beurmanni*, *S Beurmanni* var *asteroides* (Splendore) de Beurmann and Gougerot, 1911<sup>3</sup>

In 1907, Lutz and Splendore<sup>4</sup> described bizarre forms of organisms in man and in experimentally produced sporotrichosis in rats In 1908,

Studies, observations and reports from the Laboratory for Mycology of the Department of Dermatology of the Barnard Free Skin and Cancer Hospital, service of Dr M F Engman, Sr, and from the Ellis Fischel State Cancer Hospital

1 Splendore, A Sobre uma cultura de uma nova especie de cogumello pathogenico do homem, Rev Soc sc de São Paulo **3** 62, 1908

2 Splendore, A Sporotrichoses americanas, Brasil-med **23** 361, 1909

3 de Beurmann L, and Gougerot, H Les sporotrichum pathogenes Classification botanique Arch de parasitol **15** 5, 1911

Greco<sup>5</sup> described radiate formation of *Sporotrichum* in man and rats from Argentina. In 1909, in France, Harter and Gruyer<sup>6</sup> described radiate formation in a guinea pig experimentally infected with *Sporotrichum* supposedly *S. Beurmanni* (*S. Schenckii*)

In 1934, Bordes, Berhouet and Errecart<sup>7</sup> published a report of 4 cases of sporotrichosis from Uruguay. During the course of the microscopic examination of sections from 1 of these cases (a gummatous lesion), Talice noted in the hematoxylin and eosin-stained preparation the asteroid formation described by Splendore. This case and another from Uruguay were published by Talice in 1935<sup>8</sup>. In the same publication there appeared a report on the production of radiate forms in experimental sporotrichosis of the rat by MacKinnon. At the meeting of the Third International Congress for Microbiology held in New York in September, 1939, MacKinnon<sup>9</sup> reported that he and Talice had found the asteroides form of Splendore in the pus from 6 of 7 patients with sporotrichosis. They also reported finding radiate forms in rats infected with a European strain of *S. Schenckii*.

The presence of radiate or asteroid formation on cells of *Sporotrichum*, therefore is not an unusual occurrence, but it is still sufficiently uncommon to warrant interest. To date, these structures have been found chiefly in man in South America—Brazil, Uruguay and Argentina—and in experimentally infected animals in South America and in Europe—France. The literature in North America as far as we know has not to date revealed this peculiar phenomenon.

#### REPORT OF CASE

*History*—G. G., a white man aged 53, a construction worker, was admitted to the Ellis Fischel State Cancer Hospital on Dec. 14, 1944 with a complaint of a "sore" on the left hand of fourteen months' duration. He was born and

4 Lutz, A., and Splendore, A. Sobre uma mycose observada em homens e ratos. Contribuição para o conhecimento das assim chamadas sporotrichoses, *Rev. med. de São Paulo*, Reprint, 1907, *Sopra una micosi osservata in uomini e topi*. Contribuzione alla conoscenza delle costi dette sporotrichosi, *Ann. d'ig. sper.* **17**: 581, 1907.

5 Greco, N. V. Biologia del *Sporotrichum Schenckii-Beurmanni*. Etiologie y patogenia de la esporotricosis, *Rev. dermat.* **1**: 78, 1908.

6 Harter, A., and Gruyer. Formes actinomycosiques dans la sporotrichose experimentale, *Compt. rend. Soc. de biol.* **61**: 309, 1909.

7 Bordes, C., Berhouet, A., and Errecart, L. M. Cuatro casos de esporotricosis, *Bol. Soc. med. quir. del Centro de la Republica* **7**: 17, 1934.

8 Talice, R. V. Deux cas de sporotrichose produits par le *Sporotrichum* asteroïde de Splendore, *Ann. de parasitol.* **13**: 576, 1935.

9 Talice, R. V., and MacKinnon, J. E. The Asteroides Form of Splendore in Spontaneous and Experimental Sporotrichosis, in *Proceedings of Third International Congress of Microbiology* (1939), 1945, pp. 510-511.



had lived in Missouri all his life. A small red spot first developed on the thumb where a crutch, used for a broken ankle, had rubbed. His physician applied "drawing salves," but the affected area increased in size and became hard and cracked. There was no ulceration, bleeding or itching. No other member of the family had any similar lesion. Three months prior to admission, two deep (subcutaneous) nodules appeared on the left arm. One month prior to entry a third nodule became apparent. Since that time several new nodules had been noticed. There had been no loss of weight or gastrointestinal symptoms. The past history revealed numerous operations and a "nervous breakdown" because of worry in 1934. There had been the usual childhood diseases and possible malaria and rheumatic fever, but the latter diseases had not been confirmed. The family history was irrelevant.

A systemic review revealed no symptoms relative to his eruption.

*Physical Examination*—The patient was a well developed man, in no distress, weighing 155 pounds (70.3 Kg). The blood pressure was 122 systolic and 74 diastolic, the pulse rate 72 and the respiration rate 20. On the skin of the chest



Fig 1—Verrucous, granulomatous lesion of the left thumb. The arrow indicates a subcutaneous nodule.

was a diffuse, symmetrically distributed, erythematous rash which blanched on pressure. Results of examinations of the eyes, ears, nose, throat, abdomen and other organs were not remarkable. Over the dorsum of the thumb of the left hand, in the region of the metacarpal and first phalanx was a hard, horny, raised lesion of the skin with irregular, verruca-like outgrowths (fig 1). It measured 3 by 4.5 cm, was furrowed and cracked, but not ulcerated. The surrounding skin was intensely red and indurated. Extending up the forearm on the radial aspect were eight firm, rubbery, rounded areas of induration. These subcutaneous nodules did not appear beyond the elbow and were not painful or pruritic. Lymphadenopathy was absent. The clinical diagnosis was erythema nodosum.

*Course*—The patient was discharged from the hospital on December 18, four days after admission, and was readmitted on December 26. The white blood cell count was 9,500 with a normal differential count. The Kahn test was negative. The agglutination test for tularemia gave negative results. A roentgenogram of the chest did not reveal any pulmonary involvement. A roentgenogram of the thumb showed soft tissue swelling, but no evidence of bone change. Biopsy specimens

were taken from the lesions on the thumb and wrist. Microscopic examination showed a granulomatous type of lesion suggestive of tuberculosis, syphilis, tularemia or fungous infection.

On Jan 2, 1945 a nodule was excised. Part of the nodule was ground up and injected into a guinea pig, part was used for culturing and the remainder fixed, sectioned and stained for acid-fast bacteria. The guinea pig died but acid-fast bacteria were not found. A subsequent guinea pig inoculation with fresh material was also negative for *Mycobacterium tuberculosis*. The cultures were overrun with contaminants and no definite pathogenic fungus was isolated.



Fig 2—All photomicrographs made from a sporotrichotic nodule, stained with methylene blue and eosin, at a magnification of  $\times 1520$ . 1, asteroid form of *Sporotrichum* with a central, thick-walled cell surrounded by polymorphonuclear leukocytes, 2, eosinophilic, radiate form with short rays, 3, large pinkish blue-staining cell with eosinophilic material on the surface, 4, single large bluish-pink cell of *Sporotrichum*.

Between January 4 and January 23, as an antinflammatory measure, 800 r of roentgen rays was directed to the left thumb, 500 to the lower part of the left forearm and 500 to the upper part of the left forearm. The inflammation subsided somewhat, and on this basis a tentative diagnosis of Boeck's sarcoid was made.

The microscopic slides were submitted to one of us (M M) because of the possibility that the infection might be mycotic. Radiating forms were found having a central spherical cell and eosinophilic peripheral radiations. One of the structures in particular (fig 2, 1) bore a striking resemblance to that described by de Almeida<sup>10</sup> in experimental aspergillosis in the rabbit (see his fig 11). Another node was excised for further study and for the cultivation of a pathogenic aspergillus. A review of the slides resulted in the diagnosis of sporotrichosis of the asteroid type. This was confirmed by the finding in culture of the characteristic *Sporotrichum Schenckii* (*S. asteroides*).

On February 8 the patient was given a saturated solution of potassium iodide beginning with 10 drops three times a day. The dose was increased one drop daily, until on February 22 he was receiving 25 drops three times a day by mouth and topical applications of tincture of iodine. He gained 5 pounds (2.3 Kg) in weight. The nodules on the forearm and the primary lesion on the thumb became progressively smaller. When seen in the clinic on March 28, the satellite nodules had almost disappeared and the involved thumb was practically healed except for slight crusting. He was told to continue the use of potassium iodide for two weeks. He was last seen on July 18. The thumb appeared well, but several barely perceptible nodules had again appeared over the left forearm. He was again given potassium iodide.

#### HISTOPATHOLOGIC OBSERVATIONS

The diagnosis having been established by culture, it was not difficult to recognize that histologically the picture was similar to that of the usual verrucous cutaneous sporotrichosis. The epidermis showed irregular acanthosis with an elongation of the stratum mucosum in some places and a shortening in other areas to produce a pseudoepitheliomatous formation. There was intercellular and intracellular edema with a dense cellular infiltrate spread throughout most of the cutis. Scattered throughout the pseudoepitheliomatous growth in the cutis and extending into the epidermis was a prominent infiltrate of polymorphonuclear leukocytes forming microabscesses in some regions. The lymph spaces were dilated in the upper third of the cutis. In addition to the many polymorphonuclear leukocytes in the cutis there were plasma cells, young connective tissue cells, many epithelioid cells, lymphocytes, some scattered mast cells and giant cells of the Langhans type. Many small blood vessels were also seen throughout the infiltrate.

The presence of nodules in the tissue emphasized the granulomatous nature of the lesion. These nodules were usually deep in the cutis, but in some sections they were close to the epidermis. The individual nodules were characteristic of those usually seen in sporotrichosis. The central areas were made up of necrotic masses and in others small microabscesses could be seen. Surrounding the central area, usually termed the chronic suppurative zone, there were richly stained cells consisting

10 de Almeida F P. Formações radiadas da membrana dos cogumelos parasitos. Ann Fac de med da Univ de São Paulo 10 163, 1934.

of polymorphonuclear neutrophils, some eosinophils, lymphocytes, red blood cells and some macrophages. Closely adjacent to this area were many epithelioid cells and giant cells of the Langhans type. The giant cells were variable in number, size and shape and occasionally appeared in groups suggesting a tubercle. This area corresponded to the tuberculoïd zone. The outer or peripheral area of the nodule, the so-called sypiloid zone, was also characteristic of a typical sporotrichotic nodule, with plasma cells, connective tissue cells and lymphocytes. The blood vessels in the outer zone were small and increased in number. The collagen bundles were invaded by cells, chiefly lymphocytes and plasma cells. There was a perivascular reaction. Apparently as a result of the granulomatous process, the elastic fibers were irregular and broken so that the nodules appeared distinct. While many of the nodules were isolated, others were enlarged as a result of the merging of two or more nodules.

Of particular interest in the hematoxylin and eosin-stained sections were the radiating, acidophilic forms in the microabscesses of a nodule. With methylene blue and eosin these bodies appeared more distinctly as eosinophilic forms. The central cell was spherical and was surrounded by radiating, eosinophilic elongations (fig 2, 1). Scattered throughout the nodule, however, were acidophilic bodies varying in size and shape, some with short radiating structures and others without any peripheral additions (fig 2, 2 and 4). These scattered forms were usually surrounded by various cells, chiefly plasma cells and lymphocytes. The acidophilic bodies were identified as the asteroid form of *S. Schenckii*.

#### MYCOLOGY

On the basis of radiate or asteroid formation of the cells in tissue Splendore created the new species, *S. asteroides*, for the organism isolated from his case of sporotrichosis. De Beumann and Gougeot and also Matruchot examined the culture, and although the fungus to them had all the characteristics of *S. Beurmanni*, they considered Splendore's organism as a variety, *S. Beurmanni* var. *asteroides*. The latter classification was arrived at by comparing the conidia, those of *asteroides* being more fusiform, and by considering the asteroid formation as a specific characteristic.

In tissue the fungus appears in two forms. The first is a short somewhat rectangular basophilic cell measuring approximately 2 to 3 microns in its long axis. This form is similar to the cells found, but with much difficulty, in tissue of sporotrichosis when stained by the Gram method. Such cells were not seen in the tissue in the case presented herein. The second type has been designated as the asteroid form and is characterized by the presence in tissue or pus of radiate structures on the

pathogenic organism. In the tissue examined there were typical asteroid bodies having a central, spherical thick-walled (double-contoured), pink-staining cell, and measuring approximately 5 microns (some measuring 6 or 7 microns). Some of the central cells showed a blue coloration. The rays, eosinophilic staining, varied in length from 2 to 8 microns. Scattered throughout the nodule were acidophilic bodies varying in size from 6 to 12 microns, some of which appeared as young cells with short rays (fig 2, 2) while others were larger with a diffuse bluish pink color. Some of the large cells had diffuse pink material which appeared to be emanating from the wall of the cell (fig 2, 3). The radiate forms seen in the tissue were almost similar to those so well described by Splendore and also by Talice.

A portion of a biopsy specimen was planted on Sabouraud's glucose agar after the previous tissue implant had been overrun by contaminants. On the fourth day, although part of the agar slant was contaminated with saprophytic fungi, small dark brown to black colonies were seen. Isolated in pure culture, the fungus developed small cream-colored colonies which rapidly became black. Grossly, the growth was identical with that of *S. Schenckii* (fig 3, 1). The center of the colony was irregularly convoluted to cerebriform. Radial grooves extended from the central formation, but not quite to the periphery of the growth. On glucose agar the cultures subsequently developed a dark brown duvet or powdery to somewhat cottony overgrowth, which is considered by some to be a pleomorphic change. This is in accord with the observations of de Beurmann and Gougerot<sup>11</sup>. Subcultures on other media likewise did not differ from those characteristic of *S. Schenckii*.

Microscopically the cultural growth is made up of filaments and spores which closely correspond to the dimensions of those structures seen in *S. Schenckii* (*S. Beurmannii*)<sup>12</sup>. The hyphae vary from branched, interlacing, fine, threadlike, septate filaments, measuring approximately 1 to 2 microns in diameter, to pleomorphic types consisting of chains of oidoid or arthrosporous cells, approximately 3 to 5 microns in diameter. Large round cells with thick walls—chlamydospores—are seen as intercalary (within the hypha) or terminal structures measuring from 4 to 9 microns in diameter.

The conidia or spores are spherical, ovoid, pyriform or bacillary in appearance, pedicellate or sessile, occurring terminally or laterally, singly or in groups, measuring approximately 2 by 2 to 8 microns. When seen

11 de Beurmann, L. and Gougerot, H. *Les sporotrichoses*, Paris, Felix Alcan, 1912, p. 140.

12 Moore, M., and Kile, R. L. Generalized, Subcutaneous, Gummatous, Ulcerating Sporotrichosis. Report of a Case with a Study of the Etiologic Agent, *Arch. Dermat. & Syph.* **31**: 672 (May) 1935.

in groups, they may take the form of a rosette or a cluster of spores on short branches, the spores being attached to sterigmata. When growing laterally the conidia appear to be directly attached to the hypha or connected by a short pedicle from which the spore, when mature, becomes easily detached. The young conidia are hyaline, thin walled and vary in shape and size, but when mature they tend to round up to form thick-

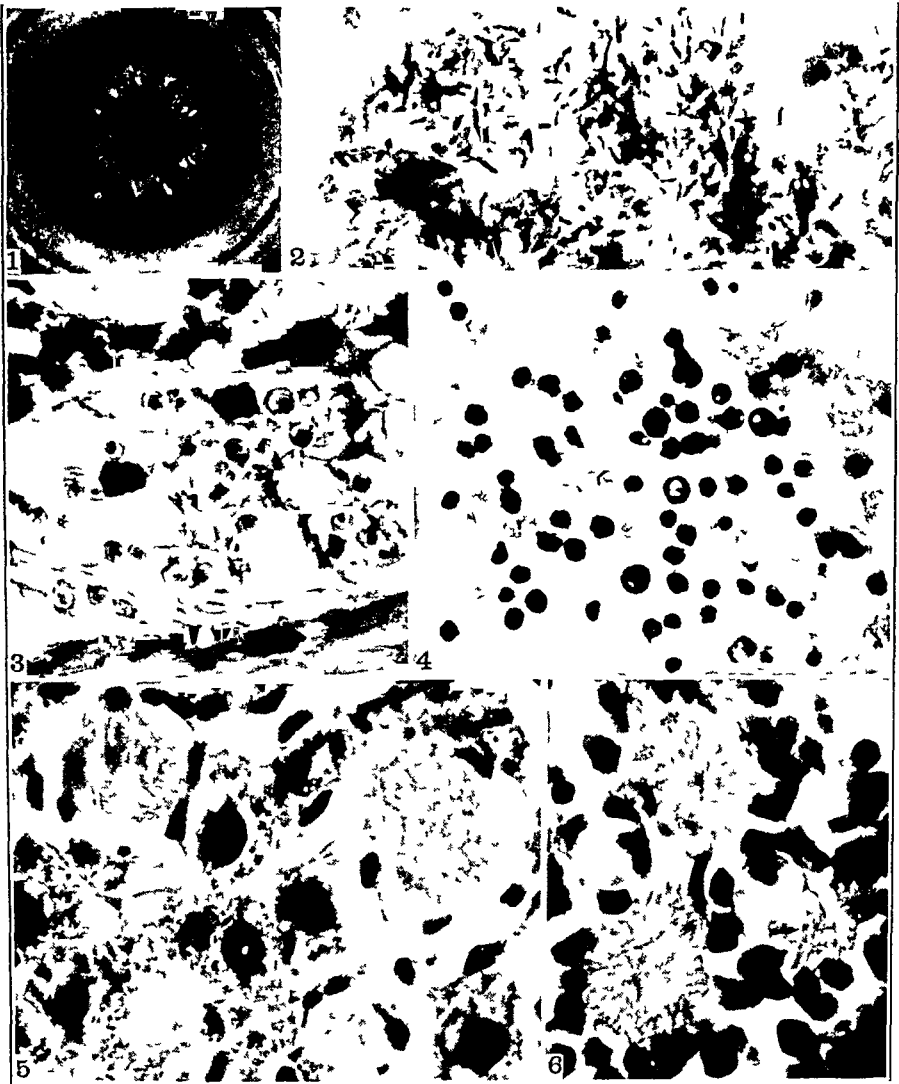


Fig 3—1, sixty day old subculture of *Sporotrichum Schenckii* (*S. asteroides*) on Sabouraud's glucose agar, 2, section of guinea pig tissue showing bacillary form of *Sporotrichum*—Gram-Weigert stain,  $\times 754$ , 3, section of mouse testis showing pink-staining spherical to ovoid cells of *S. Schenckii*—hematoxylin and eosin,  $\times 754$ , 4, section of mouse testis showing spherical to ovoid simple or budding cells—Gram-Weigert stain,  $\times 754$ , 5, section of mouse liver with radiating forms in hepatic sinusoids—hematoxylin and eosin,  $\times 677$ , 6, section of mouse spleen showing radiating structures—hematoxylin and eosin  $\times 754$

walled spherical cells, usually brown, and measure approximately 4 microns in diameter

Color is an important factor in species or at least variety differentiation. Such colors, however, in order to be of any value, should be constant or at least consistent with the strain of fungus. De Beurmann and Gougerot,<sup>11</sup> using color formation on Sabouraud's agar as a criterion, established three groups or types of organisms: alpha which shows little pigmentation, remaining white or light brown; beta, which develops a chocolate brown color; and gamma, which changes from gray to ebony black in four to five days. Although such changes in color do occur, they should not be considered as a system of classification since, as has been pointed out previously,<sup>12</sup> variations in the constituents of the medium will alter the color of the growth. The continued subculturing of *Sporotrichum* on the same medium, such as Sabouraud's glucose agar, will also cause changes in color. Furthermore, a comparison of eight strains of *Sporotrichum*, some of which had been recently isolated while others had been in the stock collection for several years, showed all the color changes on the same medium indicated in de Beurmann and Gougerot's classification. All the strains when first cultured were black. This holds true both for *S. Schenckii* and for the fungus described as *S. Beurmannii*.

A comparison was also made of the morphologic appearance of *S. Schenckii* and of strains having the characteristics attributed to *S. Beurmannii*. Except for minor differences which can invariably be found in strains of the same species, there is insufficient evidence to consider them as separate and distinct species. It is felt, therefore, that since *S. Schenckii* was the first strain described, *S. Beurmannii* should be considered as a synonym. *S. asteroides* has all the features to be found in *S. Schenckii* (*S. Beurmannii*) with the addition of asteroid formation in tissue. Asteroid or radiate formation in tissue, although a rare phenomenon in sporotrichosis, is not uncommon with other organisms such as *Actinomyces* (most species), *Coccidioides immitis*, *Aspergillus fumigatus* and others. In view of the fact that radiate formation of fungi is merely a concomitant finding in tissue and not an expression of species differentiation, it is felt that such a finding is not sufficient reason in itself for designating this strain of *Sporotrichum* as a new species or even as a variety. Consequently this organism should be *S. Schenckii*.

*Sporotrichum Schenckii* Matruchot, L. Compt rend Acad d Sc 150 543, 1910

Synonymy *Sporotrichum* sp. E. F. Smith in Schenck Bull Johns Hopkins Hosp 9:286 1898

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- Sporotrichum asteroides* Splendore, A Rev Soc sc São Paulo **3** 62, 1908, Brasil-med **23** 361, 1909
- Rhinocladium Beurmanni* var *asteroides* Vuillemin, P Compt rend Acad d sc **21** 148, 1910
- Sporotrichum Beurmanni* var *asteroides* de Beurmann, L, and Gougerot, H Arch de parasitol **15** 42, 1911
- Rhinocladium Beurmanni* Vuillemin, cited by de Beurmann, L, and Gougerot, H Arch de parasitol **15** 98, 1911
- Sporotrichopsis Beurmanni* Gueguen, cited by de Beurmann, L, and Gougerot, H Arch de parasitol **15** 103, 1911
- Rhinotrichum asteroides* Verdun, P Precis de parasitologie humaine, Paris, G Doin, 1912, Verdun, P, and Mandoul, A H ed 3, ibid, 1924, pp 714-715
- Sporothrix asteroides* Davis, D J J Infect Dis **12** 453, 1913
- Rhinocladium Schenckii* Verdun, P, and Mandoul, A H Precis de parasitologie humaine, ed 3, Paris, G Doin, 1924, pp 713-714
- Rhinotrichum Schenckii* Ota Jap J Dermat & Urol **28** 4, 1928
- Rhinotrichum Beurmanni* Ota Jap J Dermat & Urol **28** 4, 1928
- Rhinocladium Schenckii* Grandinetti, L Contribuição para o estudo da esporotricose, São Paulo, Empr Rev tribunais, 1934, p 18
- Rhinocladium asteroides* Grandinetti, L Contribuição para o estudo da esporotricose, São Paulo, Empr Rev tribunais, 1934, p 53
- Sporotrichum Schenckii* var *Beurmanni* (Matruchot and Ramond) Dodge, C W Medical Mycology, St Louis, C V Mosby Company, 1935, p 806

## ANIMAL INOCULATIONS

A ground-up, excised, subcutaneous nodule was injected intraperitoneally into a guinea pig. Death followed nine days after injection. Sections of tissue stained by the Gram-Weigert method revealed clumps of the short, somewhat rectangular cells of *Sporotrichum* occurring as individual or occasionally as joined cells (fig 3, 2).

A saline suspension of organisms made from a twelve day old subculture on Sabouraud's glucose agar was injected into 2 mice, 1 male and 1 female. It was injected intraperitoneally into the female and intraperitoneally and intratesticularly into the male. The male died one hundred and forty-three days following the injections, but the female was still alive after one hundred and eighty-two days. Autopsy was performed on the male mouse. Grossly there was no apparent change in most of the organs of the thoracic and abdominal cavities. The testes, however, were greatly enlarged and covered with small tubercle-like protuberances. Microscopically, there were necrotic nodules of varying size in



the testes The centers of the nodules showed liquefaction necrosis and were made up of leukocytes, most of them in a degenerative state The periphery of the nodule was made up of fibroblasts and then fibrosis Scattered throughout the nodule, especially prevalent in the areas of liquefaction and arranged for the most part in clumps, were large numbers of spherical, simple or budding yeastlike cells, measuring from 4 to 8 microns in diameter In sections stained with hematoxylin and eosin these cells were pink or eosinophilic (fig 3, 3) In the methylene blue and eosin sections, the central area of the cell appeared blue, whereas the wall took the eosin stain When stained by the Gram-Weigert method, the yeastlike organisms were deep purple (fig 3, 4) No radiate or asteroid forms were seen in the testes

The lungs and kidneys did not contain organisms In the liver there was an infiltrate of leukocytes in areas around the margin In the hepatic sinusoids there were radiating structures of various sizes (fig 3, 5) It was difficult to determine with complete satisfaction whether these bodies represented the typical asteroid forms of sporotrichosis These bodies were eosinophilic, but no central fungus cell similar to that seen in human tissue or to those seen in the testes could be found by various staining procedures The radiations did, however, appear to emanate from the central region The spleen appeared somewhat larger than normal Microscopically, there were many areas of necrosis, especially evident close to the capsule Radiating forms similar to those seen in the liver were found in the spleen (fig 3, 6) The radiations here too seemed to emanate from the central region of the structure Several nodes taken from the mediastinal region did not appear normal, but microscopically they showed only inflammation

#### SUMMARY AND CONCLUSIONS

A case of granulomatous, verrucous sporotrichosis of the left thumb with a subsequent lymphatic spread in the form of subcutaneous nodules is presented Microscopically, sections of nodules were characteristic of sporotrichosis The finding of acidophilic radiating structures in a nodule of the tissue at first suggested aspergillosis The cultivation of a *Sporotrichum*, however, established the diagnosis of sporotrichosis with asteroid formation in tissue The fungus first named *Sporotrichum asteroides* by Splendore then *S. Beuermannii* var *asteroides* by de Beuermann and Gougeiot when studied in detail, appears similar to, if not identical with strains of *S. Schenckii* On the basis of comparative studies with eight strains of *Sporotrichum* it was concluded that the strain showing the radiate structures in tissue should be classified as *S. Schenckii* Asteroid formation was not observed in a guinea pig into which tissue was injected Instead the characteristic bacillary form was

seen in tissue sections stained by the Gram-Weigert method. In a mouse into which was injected a suspension of organisms from a twelve day old subculture of the fungus, ovoid to spherical, simple or budding, yeast-like cells were found in the testes. Radiate structures were found in the liver and spleen, but their nature was not definitely ascertained. Because of the finding of radiating structures on fungi in other diseases, it may be concluded that asteroid formation in sporotrichosis should be considered as a concomitant, although uncommon, finding. The finding of such structures in tissue is insufficient reason in itself for the establishment of either a different species or a different variety.

## CONTACT DERMATITIS

An Analysis or Tabulation of All Cases Proved In a Single Year

J B HOWELL, M D

DALLAS, TEXAS

**I**N human beings, eczematous dermatitis is possibly the most common of all recognized allergic diseases"<sup>1</sup> It is an entity which may be caused by many unrelated substances In our private practice Dr Bedford Shelmire and I kept notes for a period of one year on all patients with contact dermatitis in whom the offending allergen or allergens were discovered The purpose of this paper is to present the unusual features of a few of these cases, to point out the common sensitizing substances found to be peculiar to some specialized trades, and to emphasize the frequent occurrence of sensitization dermatitis from topical medications

All cases presented represent proved examples of eczematous contact dermatitis In each case the opportunity for exposure to the substance or substances was demonstrated, an eczematous reaction followed patch tests with harmless concentrations of the material in question and elimination of the substances which elicited the positive reaction resulted in a disappearance of the dermatitis A large number of patients seen during the same period of time unquestionably had contact dermatitis but could not be included in this series because all the previously mentioned postulates could not be fulfilled

None of the numerous instances of dermatitis venenata from poison ivy are included or is any attempt made to show statistically the place of eczematous contact dermatitis in relation to other dermatologic disorders During the twelve month period, we were able to prove the cause of contact dermatitis in 250 cases

### CONTACT DERMATITIS FROM TOPICAL APPLICATIONS

The cause of eczematous contact dermatitis was found to be topical medicaments more frequently than any other single group of allergens Some estimation of the likelihood of sensitization from specific drugs can be obtained from a summary (table 1) of the proved cases Sulfonamide compounds and mercurials in topical application rank as the most potent sensitizing agents and therefore the preparations most likely to

<sup>1</sup> Sulzberger, M B Dermatologic Allergy, Springfield, Ill, Charles C Thomas Publisher, 1940, p 89

cause contact dermatitis. If a person is sensitized to merthiolate for example, he may or may not be found to be allergic to ammoniated mercury and/or mercury bichloride. He, therefore, may be sensitive to only a few or to many of the mercurial drugs. On the other hand, if a patient is sensitized to sulfathiazole, he is likely to be hypersensitive to other sulfonamide preparations.

TABLE 1—*Contact Dermatitis from Drugs*

Drugs	Number of Cases
<b>Mercurials</b>	
Ammoniated mercury	14
Mercury bichloride	3
Oleate of mercury (merceresol)	2
Merthiolate	2
Mild mercurous chloride (dusting powder)	1
Solution of merbromin	1
Neko soap (potassium mercuric iodide)	1
Mercuric salicylate	1
<b>Total</b>	<b>25</b>
<b>Sulfonamide compounds</b>	
Sulfathiazole ointment	19
Sulfadiazine ointment	2
Sulfanilamide (powder)	3
<b>Total</b>	<b>24</b>
<b>Tars</b>	
Solution of coal tar	5
Crude coal tar	4
<b>Total</b>	<b>9</b>
<b>Resorcinol</b>	<b>5</b>
Benzocaine—contained in Folle Derma Medicone, Korium, and Calagesic ointment	4
Butesin picrate	4
Quinolol	2
Nupercaine hydrochloride	2
<b>Other drugs and preparations</b>	
Hydrophen (orthophenylmercuric nitrate)	1
Acetarson (powder)	1
Butacaine sulfate	1
Sulfur (ppt)	1
Metycaine hydrochloride	1
Calmitol	1
Mazon	1
Zemo lotion	1
Tannic acid	1
Resinol ointment	1
Prescription (active ingredients: resorcinol, phenol, juniper tar)	1
Formaldehyde	1
<b>Total</b>	<b>12</b>

An interesting feature of sensitization to tars presented itself. It was observed that patients who become sensitized to crude coal tar were also hypersensitive to solution of coal tar. The reverse is also true, except for the rare possibility that a person using solution of coal tar will become sensitized to the vehicle alcohol or the quillaja rather than to the coal tar. Solution of coal tar contains coal tar, 200 Gm, quillaja, in moderately coarse powder, 100 Gm, and alcohol in sufficient quantity to make 1,000 cc.

Sensitization dermatitis from topical medicaments following the treatment of some trivial eruption, as pruritus, miliaria, a superficial

burn, an insect bite, poison ivy dermatitis, sunburn or "athlete's foot," is a common and everyday occurrence. When contact dermatitis occurs during the course of topical chemotherapy, the common mistaken interpretation is that infection, such as erysipelas or cellulitis, has occurred or that the patient has contracted poison ivy dermatitis.

The following case summaries are included to illustrate sensitization dermatitis from the topical application of drugs.

CASE 1—On the seventh postoperative day following a herniorrhaphy in the right inguinal region, both the surgeon and the patient noted a slight erythematous swelling and weeping at the site of the healing wound. A serous drainage was observed on the dressing. A diagnosis of infection was entertained, and a 10 per cent solution of merbromin was applied twice daily. During the next three or four days the dermatitis became more intense and covered a wider area than before. On examination of the operative site, the eruption was found to involve an ever widening rectangular area which conformed exactly to the site being treated with merbromin. It was apparent that the patient was allergic to this substance. Merthiolate had been used to prepare the skin before operation. Unquestionably, that application was the sensitizing exposure, because a seven day interval, the period of incubation of sensitivity, preceded the onset of this eruption. Patch tests elicited positive reactions to both merthiolate and merbromin. The dermatitis healed rapidly after the use of merbromin was discontinued.

CASE 2—J. H. was given chlorohydroxyquinoline ointment for local application to a small area of folliculitis on the back of the neck. At the end of ten days' treatment, the eruption had improved only slightly. A 6 per cent bismuth tribromphenate ointment was then prescribed. This was applied for twenty-four hours, and the following morning an acute contact dermatitis of the neck was noted by the patient. He was greatly displeased, thinking that the new ointment was "too strong." From his history, it was learned that he had never used bismuth tribromphenate or chlorohydroxyquinoline before. Patch tests with these two preparations elicited a strongly positive reaction to the latter and a negative one to the former.

This case illustrated an example of sensitization dermatitis in a patient who was in the process of acquiring sensitivity to chlorohydroxyquinoline (in the incubation period of sensitization) when a new drug was started. Obviously stopping the drug at that point would not have prevented the development of the allergic reaction.

CASE 3—C. M. C., a truck driver, received a superficial cut on the dorsum of the right hand and the fourth and fifth fingers. Sulfanilamide powder was used locally for approximately nine days. At this time an erythematous and finely vesicular dermatitis appeared over the treated sites. The physician, observing the hand at this period, made a diagnosis of cellulitis. Hot wet compresses alternated with sulfathiazole ointment were prescribed. The eruption progressed to involve the lower half of the forearm and the exposed parts of the face, neck, ears and left arm. In this patient there developed both a sensitization and a general photosensitivity to sulfonamide compounds. He also exemplified group sensitization, being hypersensitive to both sulfanilamide and sulfathiazole.

Use of patch tests with sulfonamide drugs on patients who are sensitive to the compounds is not without danger especially in persons who

are photosensitive. Because of our previous experience with several cases of accentuation of existing eruptions which followed positive reactions to patch tests, contact testing with sulfonamide drugs was largely discontinued before this study was started. We have found that

TABLE 2—*Contact Dermatitis Due to Occupational Allergens*

Occupation	No. of Cases	Areas Involved	Allergens
Worker preparing carrots for dehydration	1	Hands, forearms	Carrots
M D, general practice	1	Fingers	Procaine hydrochloride
M D, surgeon	1	Hands	Rubber gloves
Worker in aircraft industry	1	Hands, forearms	Rubber gloves
Highway construction bridges, etc., working with lumber treated with creosote	1	Face, hands, forearms	Creosote
Construction worker contacting posts and telephone poles treated with creosote	1	Face, neck, chest, arms	Creosote
Workers in aircraft industry contacting plastics	4	Face, arms, hands	Formaldehyde
	1	Face, arms, hands	Phenol formaldehyde resin
Workers in aircraft industry contacting plywood	3	Hands, forearms	Glue (possible formaldehyde sensitivity)
Aviator	1	Ears	Rubber earcup
Baker	1	Fingers, hands	Cinnamon
Worker in aircraft industry	1	Face, neck, eyelids, hand	Naptha
Printer of photographs	1	Tips of fingers 1, 2, 3 left hand	Turpentine
Men dipping lumber in a chemical solution called "sealer" before shipping to tropics	2	Hands, arms, ears, face, neck	"Sealer"
Dental technicians who prepare false dentures	1	Finger tips	Carbon tetrachloride
	1	Finger tips	Ethylene glycol
'Car hop' at root beer stand	1	Hands, forearms	Chlorine
Glasses and mugs were dipped in chlorine solution for cleaning			
Worker in industry, manufacturing tents for military use	1	Hands, forearms, face	Olive drab cloth
Workers for cleaning and polishing Greyhound Bus Company	2	Hands	Johnson cleaner
Workers in blueprint industry manufacture of ice	7	Hands, face, eyelids	Bichromate
Workers in aircraft industry	10	Hands, face, neck, forearms, eyelids	Zinc chromate primer
Farmers, ranchers, oil field workers	35	Exposed areas face, legs, arms	Weeds
Worker washing containers into which honey was extracted	1	Hands, face, neck, forearms	Honey and beeswax
Nurses, housewives	3	Hands, face, eyelids	Primrose plant
Barber	1	Backs of hands, fingers	Bay rum
Housewife	1	Hands, arms, face	Citronella
Housewife	1	Face, neck, forearms	Flit
Housewife	1	Right hand, lips, eyelids	Cocobolo wood

the oral administration of a small dose (1 grain [0.06 Gm.]) of the sulfonamide drug in question is serviceable in proving specific sensitization. Positive reactions to patch tests were noted in this series in only 2 of our 23 cases, and proof of sensitivity was confirmed by oral test doses in 2

other cases. In 9 cases the reactions were recorded as unquestionable sensitization to sulfonamide compounds and in 10 other cases as eruptions most likely due to sulfonamide compounds.

#### CONTACT DERMATITIS OF OCCUPATIONAL ORIGIN

There are many occupations in which persons are exposed to the hazard of contact dermatitis (table 2). In the Southwest, eczematous contact dermatitis from sensitization to vegetation is a common occurrence (table 3). This type of eruption is not a disease affecting solely one occupation, yet contact dermatitis from weeds must be considered an



Fig 1—Contact dermatitis in aviator, from rubber ear cups

occupational hazard among farmers, ranchers, workers in the oil fields and others. Persons living solely in large metropolitan areas rarely have dermatitis from weeds. Those who have contact with weeds only infrequently may become hypersensitive however. A severe widespread eczema due to weeds was observed in a banker who had contact with vegetation only while hunting, fishing and golfing. One of our patients with a most extensive eruption was a man whose occupation was that of sheriff. Two cases have been observed in which the patients were ministers who held services in rural areas during the summer months. Another patient is a dentist whose hobby is cattle raising. He makes contact with vegetation while riding horseback to inspect his herd on week ends and after office hours.

TABLE 3—Reactions to Patch Tests with Oleoresins of Weeds

Weed	Case Number																																				
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	Total	
<i>Iva angustifolia</i> (Narrow leaved marsh elder)	+	+				+	+		+						+	+						+		+	+	+	+	+	+	+	+	+	+	+	+	+	18
<i>Helenium tenuifolium</i> (Bitterweed)	+	+	+	+		+	+		+	+	+	+		+		+	+	+						+		+	+	+	+	+	+	+	+	+	+	+	20
<i>Ambrosia elatior</i> (Short ragweed)	+	+	+	+	+	+	+		+	+	+		+	+		+	+		+				+	+	+	+	+	+	+							+	23
<i>Helenium microcephalum</i> (Sneezeweed)	+	+	+			+	+		+	+	+	+	+	+		+	+			+				+	+	+	+			+	+	+	+	+	+	+	20
<i>Parthenium hysterophorus</i> (Santa Maria feverfew)	+		+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	24
<i>Xanthum speciosum</i> (Cocklebur)							+													+	+	+	+												+	6	
<i>Iva axillaris</i> (Lesser marsh elder)	+													+						+								+								+	1
<i>Pyrethrum</i> (Chrysanthemum)	+	+												+							+							+							+	+	7
<i>Ratibida columnaris</i> (Coneflower)	+	+																																		+	1
<i>Medicago hispida</i> (Bur clover)	+																																				1
<i>Agrostis alba</i> (Red top)	+																																				1
<i>Grindelia squarrosa</i> (Gumplant)	+																																				1
<i>Artemisia mexicana</i> (Common wormwood)	+						+																														2
<i>Eupatorium serotinum</i> (Boneset)	+																																				1
<i>Chenopodium botrys</i> (Jerusalem oak)	+		+																																		2
<i>Acanthocephalus</i> (Illinois mimosa)	+																																				1
<i>Amphicarpis dracunculoides</i> (Broomweed)	+																																				1
<i>Amaranthus blitoides</i> (Prostrate amaranth)	+																																				1
<i>Amaranthus retroflexus</i> (Red root pigweed)	+																																				1
<i>Solidago serotina</i> (Late goldenrod)	+																																				1
<i>Thelasma gracile</i> (False coreopsis)	+																																				1





The history of the course of a dermatitis from weeds is usually easily obtained and is characteristic. The eruption frequently commences on the areas of the ankles, with an onset usually in early spring. As the season progresses, the backs of the hands, forearms, face, eyelids and neck become involved. The eruption may progress to involve the entire exposed surfaces of the body. After frost kills all the vegetation, the eczema slowly clears. The patient usually remains well throughout the winter months. Acute exacerbations during this period have been seen from contact made with weed-contaminated hay and other foodstuffs. The dermatitis reappears with the return of vegetation in the spring. Each year the eczema becomes more extensive, subjective symptoms are more annoying, and the dermatitis requires a longer time to clear after the vegetation dies. The diagnosis "ragweed dermatitis" should be reserved for those in which a sensitivity to ragweed alone is demonstrated. A polyvalent sensitization occurs more frequently than hypersensitivity to a single weed. An example of an unusual case of polysensitivity to weeds was that of a rancher who was found to give positive contact reactions to forty different weeds (case 1 table 3). Only five reactions were strongly positive. The others were definite but mild. The slight reactions may be interpreted as evidence of minimal sensitivity to those specific plants. Continuous contact with those particular weeds would probably result in a mild eczematous dermatitis.

In cases of sensitization dermatitis due to weeds, only two methods of management are possible. These are (1) absolute avoidance of vegetation and (2) hyposensitization with the specific weed oleoresins. In persons who can avoid vegetation by giving up some hobby, as golfing or hunting, or in others for whom change of occupation is possible, the dermatitis will clear completely and remain well. The majority of persons in whom dermatitis due to weeds develops are farmers and ranchers who cannot avoid vegetation if they carry on their work. The oral administration of specific weed oils to understanding cooperative persons has proved to be of unquestioned value in the majority of our cases. Enough protection is afforded by this method of increasing one's tolerance to allow a continuation of the patient's occupation. The specific oleoresins should be taken during the winter months and repeated yearly.

The following are unusual cases of contact dermatitis of occupational origin. Rare examples of dermatitis from vegetation, usually occupational, are those from woods, vegetation oils and extracts.

The primrose plant blooms from December through March. It is often presented as a floral gift to hospitalized patients, as a birthday greeting and on other special occasions, such as Valentine's Day. Contact dermatitis from the primrose plant is said to occur frequently among florists. Morphologically, primrose and ivy dermatitis are indistinguish-

able. I should like to point out that dermatitis venenata from the primrose also occurs frequently in nurses and housewives.

CASE 4—Mrs F M, a housewife, made a habit of pouring water with her right hand into a pot containing a primrose plant, while she protected the blossoms by bending the flowering portion of the plant to one side. The dead leaves and stems were pruned with the fingers of her left hand. A unilateral vesicular eruption of



FIG 2—Contact eczema of upper lip and right palm from cocobolo wood (case 5)

the fingers and the palm resulted. The striking resemblance of this eruption to dyshidrosis was noted. Proving the diagnosis of dermatitis due to the primrose is usually easily done by employing an extract of primrose for patch testing or by lightly streaking a crushed leaf on a suitable test site. The unusual feature of this case was the limitation of the eruption to the lateral margins of the fingers and palm of the left hand.

CASE 5—Mrs J K consulted us because of a recurrent eczematous dermatitis involving the eyelids and perioral sites and a healing vesicular dermatitis of the fingers and palmar surface of the right hand. Acute attacks of this eruption occurred while the patient was away from home as well as while at home. Absolutely no clues regarding the cause of this eruption could be got from a lengthy conversation with the patient. She had discontinued use of nail lacquer, hair tonics, wave sets, all cosmetics, drugs (local and oral) and perfumes. Patch tests for sixty common flowers, seven weed oleoresins and six drugs commonly employed in topical medications elicited negative reactions. A twenty-four hour covered patch test, a small quantity of cocobolo wood shavings being used, produced a vesicular response on the right forearm. A focal flare-up involving the eyelids and circumoral sites and the right hand, characterized by an erythema, edema with fine vesiculation and pruritus occurred. The eruption became severe enough to necessitate continuous wet compresses and confinement to bed for several days.

This patient apparently became sensitized to cocobolo wood by contacts with knife handles made of this wood, which she used in her kitchen. When away from home she frequently contacted this allergen because she often ate steak and was

TABLE 4—*Contact Dermatitis from Wearing Apparel*

Item	Number of Cases
Nickel (rings, jewelry, glasses, underwear snaps, strap adjusters, etc.)	6
Khaki clothing	2
House shoes	1
Brown nylon sock (real silk brand)	1
Sock supporters (leather portion)	1
Stockings of nylon (redyed)	1
Glasses (plastic slip on temple piece)	1
Miscellaneous contact allergens	
Matches	1
Toilet seat	1
Adhesive tape	1
Green dye in patch testing set of common vegetables	1
New golf glove	1

given a heavy steak knife with a cocobolo wood handle. She has remained well since avoiding knives with cocobolo wood handles.

CASE 6—J S presented a typical contact dermatitis of two weeks' duration, involving the face, eyelids, neck, arms and hands. The eruption had the appearance of a dermatitis from weeds. A similar eruption had been experienced six months prior to the present attack. The patient worked in a plant where honey from different parts of the United States was collected, the honeycomb extracted and the syrup blended for marketing. He contacted both the honey and beeswax (honeycomb) daily. The honey being extracted at the time of the present dermatitis was from Iowa. Patch tests with the Iowa honey and beeswax elicited strongly positive reactions, while tests on two controls elicited negative reactions. This man was found to react only to Iowa honey. Contact tests with honey from three other localities elicited negative reactions. Patch tests were made with oleoresins from sixty common flowers and one hundred and twenty different weeds in an attempt to find out whether the patient was allergic to pollen or to some plant substance transported to the honey by the bees. No positive reactions to the plant oils were obtained. Investigation of company records revealed that honey collected from Iowa was being extracted and blended at the time of the patient's first attack of eczema, several months prior to the present eruption.

CASE 7—H B, a barber by trade, consulted me because of chronic eczema on the fingers of both hands. At his first visit, he brought for testing purposes approximately thirty different materials that he commonly used. They included several brands of hair tonics, shampoos, powder, creams, shaving and hand lotions, bay rum, etc. All patch tests elicited negative reactions, except the test with bay rum, which was found to elicit a consistently positive reaction. This solution



Fig 3—Contact dermatitis on finger tips of dental technician, due to ethylene glycol

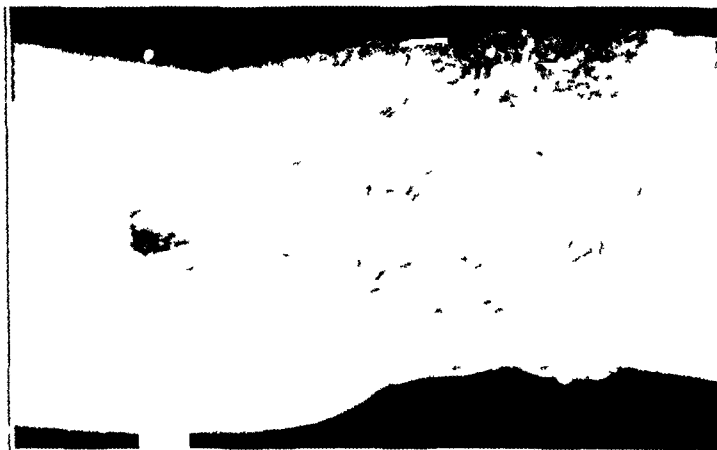


Fig 4—Dermatitis venenata, from adhesive tape used for sprained wrist

was used by the barber in a lotion which he applied to his hands after frequent washings. Discontinuing the use of the hand lotion brought about a permanent remission of the eczematous eruption.

Two similar cases of eczematous contact dermatitis in barbers from this cause were encountered approximately one year before. Bay rum

should be considered a frequent cause of contact dermatitis of the hands in barbers

CASE 8—Mrs M C, a dentist's assistant, was seen with a chronic fissured and thickened eczema of the finger tips, involving chiefly the right thumb, index finger and middle finger. The patient spent much of her time in helping to prepare artificial dentures. Patch tests were made with the various materials used in preparing false teeth. Hypersensitivity to carbon tetrachloride was demonstrated. The eruption cleared slowly, and the patient recovered completely after a substitute for carbon tetrachloride was employed.

A second dental technician was seen with an eczema of the finger tips of both hands. The sensitization dermatitis was proved to be due to

TABLE 5—*Sensitization Dermatitis from Cosmetics*

Cosmetics	Number of Cases
Nail polish (clear and colored)	20
Hair lacquer	
Hubere lacquer (pads)	21
Lacquer (spray)	
Nutrine brand	3
Renee	2
Henri Maison	2
Wavelak	1
Total	29
Lipstick (dye)	1
Eyelash dye	
Roux brand	1
Brand unknown	1
Total	2
Shampoo (Fitch)	1
Chamberlain's Lotion	1
Harriet Hubbard Ayer Skin Lotion	1
Ra-Lo Lotion	1
Tussy's Cold Cream	1
Hair rinse (brand unknown)	1
Cold permanent wave (Helené Curtis Preliminary Solution)	1

ethylene glycol which was used in the preparation of artificial dentures. Avoidance of this chemical in his work resulted in the cure of the patient's eruption.

CASE 9—J F, a truck driver, presented a pruritic eczematous eruption on the greater portion of the entire body. The face and hands were uninvolved. Thickened weeping areas were noted over the base of the neck posteriorly, in the axillas and popliteal regions and along the waist line. After approximately two or three months' observation, the possibility of khaki clothing as a cause of this dermatitis was considered. A forty-eight hour patch test with khaki elicited a questionable positive reaction. The patient was hospitalized for seven days, and his dermatitis improved strikingly. A khaki shirt was then worn part of one day. The eczematous eruption reappeared over the areas contacted by the shirt. The patient has remained well since substituting other work clothing for khaki.

CASE 10—E. B, a cafe owner, while being treated for pyoderma of the hands, requested an investigation to determine whether he was hypersensitive to lettuce

or tomatoes. Patch tests, using 1 drop of an extract of tomatoes and of lettuce, were made. The solutions employed were part of a commercial set of vegetable extracts. A fine vesicular eruption appeared at the sites where the test patches with the two extracts were applied. Contact tests with fresh lettuce and tomatoes elicited negative reactions. A search was made for the reason of the false positive reactions to the lettuce and tomato extracts. It was learned that acetone was used as a vehicle in preparing the vegetable extracts, and a small quantity of green dye was incorporated to mark the site of the test. The patient was found by patch testing to be hypersensitive to this green dye. A similar incident of sensitivity to the green dye in the set of weed extracts had been observed two years earlier.

## News and Comment

**Vacancies in the United States Public Health Service**—Appointments to fill vacancies in the Reserve Corps of the United States Public Health Service are now being made, and examinations for appointments to the Regular Corps will be held in April and May, Surgeon General Thomas Parran announced today.

Pay and allowances, established by law, are identical with those for medical officers of the Army. All traveling expenses, including travel to the first station, are paid by the Service.

In announcing the recruitment campaign, Dr. Parran stated that the opportunities for professional growth and development are almost limitless. There is clinical work in Public Health Service hospitals throughout the country. Opportunities for research exist in both laboratory and field.

Appointments to the Reserve Corps are made on a basis of review of data furnished by the applicant. Physical examination is required.

Appointments to the Regular Corps require appearance before a Board and a written professional examination. Dates and places for the examination will be announced shortly.

Those interested either in immediate appointment in the Reserve Corps or in taking the examination for the Regular Corps should request application forms from The Surgeon General, United States Public Health Service, Federal Security Agency, Washington, D. C.

**American Academy of Dermatology and Syphilology**—The American Academy of Dermatology and Syphilology will hold its next meeting on Dec. 8 to 12, 1946, in Cleveland, Ohio.

Applications for membership can now be made. Dermatologists wishing to apply for membership may secure necessary information by writing to the secretary, EARL D. OSBORNE, Secretary, 471 Delaware Avenue, Buffalo, N. Y.

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### CORRECTION

In the article by Dr. Erien Urbach and Dr. John W. Lentz entitled "Carbohydrate Metabolism and the Skin" in the November-December issue (*ARCH. DERMAT. & SYPH.* 52:301, 1945) the words 'blood' and 'skin' in the heading of the third column of table 1 were inadvertently transposed. The heading should read: Skin/Blood Sugar Ratio.

## KERATOSIS BLENNORRHAGICA

### Its Response to Penicillin

MAJOR RICHARD EMMET

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A SEARCH of the available literature reveals no record of the use of penicillin in the treatment of keratosis blenorragica. For this reason it seems desirable to report a case in which intramuscular injection of penicillin was followed by cessation of all symptoms and clearing of the cutaneous lesions.

#### REPORT OF A CASE

*History*—A white soldier, 21 years old, single, was admitted to the Station Hospital on Feb 1, 1944, complaining of a painful foot and pain and swelling of the left knee. His previous history was not remarkable, except that he had been treated with sulfadiazine for gonorrhea on an ambulatory basis from Jan 5, 1944 to January 10. The pain in the foot and the swelling of the knee followed a hike of 5 miles (8 kilometers). The patient reported to the infirmary and was sent to the Station Hospital with a diagnosis of a possible march fracture.

*Clinical Examination*—There were no abnormalities except considerable effusion in the left knee and pain and stiffness on deep bending of the knee and pes planus, second degree, with slight flattening of the metatarsal arch. The temperature was 99.4 F, and the pulse rate was 100. Roentgen examination of the foot did not reveal fracture.

*Diagnoses*—The working diagnoses were (1) second degree symptomatic pes planus, (2) acute traumatic nonsuppurative synovitis of the left knee, secondary to continued walking on the side of the foot during a march, (3) rheumatic fever and (4) acute infectious arthritis.

*Course*—The patient was treated with rest in bed and hot packs to his knee, with almost complete recession of the effusion in the knee joint. Six days later, on February 7, a urethral discharge was noted. The smear was positive for gonococci, and the patient was given sulfadiazine. He received 12 Gm in the first twenty-four hours and then 1 Gm every four hours day and night for nine more days. The discharge continued, however, and after several days of rest he was again given 12 Gm of sulfadiazine in twenty-four hours, followed by 1 Gm every four hours day and night for four more days. The urethral discharge stopped. Meanwhile, however, the pain in the knee continued, and on February 28 swelling of the right wrist was noted. At this time his temperature ranged from 98.6 to 100 F. The white cell count was 12,300, and the sedimentation rate was 100 mm per hour. He was transferred to the arthritis ward and given salicylates by mouth and heat was applied to his knee. The impression was that he had an acute infectious arthritis. The disease continued, and by the middle of March, six weeks after admission, the pains in the joints were becoming migratory, involving both knees and the left ankle, right hand and the right wrist. On March 20 bullae were noted on both knees and were considered by the ward officer to be toxic erythema.



More vesicles and bullae appeared, and some of the older ones became pustular and then crusted. On March 29 I was called to see the case in consultation. On the feet, legs and thighs, in decreasing order of severity, on the lower part of the abdomen and on the forearms and hands were many vesicles and pustules, and large numbers of discrete hornlike lesions, varying from 0.5 to 3 cm in diameter. The hornlike character was particularly noticeable on the toes and feet. Tenderness and swelling of the left knee joint were present. When some of the crusts were pulled off, a grayish pink, slightly oozing surface was noticed. The diagnosis of keratosis blennorrhagica was readily made. A biopsy specimen was taken from one of the lesions of the foot for confirmation, and the histologist, Major Ralph C. Ellis, reported as follows:

"The specimen consists of a roughly oval portion of skin measuring 12 by 9 mm in size. In the central portion there is an area 7 mm in diameter in which



Fig. 1—Keratosis blennorrhagica, just prior to administration of penicillin. Note effusion of knee joint. (Photograph by U. S. Army Signal Corps.)



Fig. 2—Just prior to administration of penicillin. (Photograph by U. S. Army Signal Corps.)

the superficial layer has been split off and has separated from the underlying skin. Attached to this area at one side is a cone-shaped top of keratinized material which is almost completely separated from the skin. Microscopic section shows a portion of the skin with extensive hyperkeratosis and parakeratosis near the center. A thick keratinized cap has separated from the central portion and is seen separately. It contains large numbers of nuclei and portions of polymorphonuclear leukocytes. In the remaining intact skin there is one small vesicle-like space between the epithelium and the underlying keratin. The epidermis itself is hyperplastic with branching proliferating pegs extending down and in the superficial dermis. In the superficial epidermis the cell outlines are loose and large numbers of polymorphonuclear leukocytes are seen embedded within the epithelium. The dermis contains many inflammatory cells, chiefly mononuclear in

type They are scattered diffusely beneath the epidermis, although at the lateral margins they have a perivascular arrangement"

The diagnosis was keratosis blennorrhagica

Prostatic massage was done but the smear showed no gonococci It did, however, contain many polymorphonuclear leukocytes Some of the hornlike nodules on the skin were removed, and smears were made from their bases but did not show any gonococci

On April 3 the patient was given penicillin intramuscularly, the initial injection being 40,000 units, followed by 20,000 units every three hours for a total of 200,000 units (twenty-four hours) No local treatment, not even soap and water, was used Two days later new vesicles were still appearing, but on April 6 no further lesions were noted and those present began to dry and fall off The articular pains became much less severe on April 7, and on April 11 the patient began to sit up in a chair, five days later he was walking around the ward, although with a little difficulty On April 14 his temperature, which had been varying from 99 to 101 F, returned to normal, and remained that way All lesions had disappeared by April 16 The patient was kept in the hospital, ambulatory, for one more month to regain his weight and the use of the muscles of his legs He was then discharged to the reconditioning unit and was last seen on June 6, by which time he had completely regained his weight and had been making 15 mile (24 kilometers) marches without difficulty

#### SUMMARY AND CONCLUSIONS

A soldier had keratosis blennorrhagica with all the classic features of gonorrheal urethritis In a few weeks monoarticular arthritis appeared together with a recurrence of the urethritis This was followed by migrating polyarticular involvement associated with typical cutaneous lesions

No gonococci were found in the cutaneous lesions, but they were recovered from the urethral discharge before treatment was begun with sulfadiazine

Administration of penicillin intramuscularly without any local therapy caused cessation of all symptoms, including pyrexia, swelling of the joints and pain, and clearing of the cutaneous lesions Although cultures for gonococci were not obtained, for technical reasons, the cure of the patient is presumed since there has been no recurrence for two months, even after hard physical exercise

## THEOPHYLLINE ETHYLENEDIAMINE AS AN ANTIPRURITIC AGENT

Preliminary Report

ERVIN EPSTEIN, M D

OAKLAND, CALIF

ALL dermatologists, in fact all practitioners, are confronted frequently by patients with severely pruritic eruptions that fail to respond to the usual therapeutic agents. Such patients are a burden to their physician, to their family and to themselves. Besides leading to loss of weight, severe psychoneuroses or other manifestations their ailment may even eventuate in suicide. Therefore this preliminary report is offered on the as yet imperfectly understood action of theophylline ethylenediamine in the immediate relief of generalized and localized itching. The results are so dramatic as to warrant extensive research on this subject.

Theophylline ethylenediamine has been employed by intravenous injection in the treatment of patients with asthma and other diseases since 1940<sup>1</sup>. Most authors feel that the use of the drug is safe when it is administered by this route. While the immediate symptoms, such as dyspnea, flushing, tachycardia and prickly sensations in the mouth and skin are disconcerting, serious complications due to administering the drug were not reported in human beings until 1943<sup>2</sup>.

### TECHNIC OF TREATMENT

So far, theophylline ethylenediamine has been unquestionably and uniformly effective in relieving itching only when it is injected intravenously. The usual technic consists of the very slow injection of 0.5 Gm. of the drug in 20 cc. of fluid. The rate of injection can be controlled by the use of a 25 gage needle. The speed of injection can also be controlled by the incorporation of the dose in 1,000 cc. of 5 per cent or 10 per cent solution of dextrose. If this is done the results are not as dramatic and not as uniform as those obtained with the syringe method, an aspect which will be discussed later in this report.

It should be emphasized that the injection must be given very slowly. The drug is dangerous when given intravenously, and speed shock must be avoided.

1. Herriman G. and Amesworth M. B. Successful Treatment of Persistent Extensive Dyspnea 'Status Asthmaticus'. *J. Lab. & Clin. Med.* **23** 135 (No. 1) 1937 cited by Cerrit.

2. Merrill G. A. Anaphylactic Deaths, *J. A. M. A.* **123** 1115 (Dec. 25) 1943.

## RESULTS

The method was first suggested to me by Kruetzer<sup>3</sup> He told of treating a patient for bronchial asthma with the intravenous injection of theophylline ethylenediamine The patient also had a severe poison oak dermatitis and noted immediate cessation of the itching Kruetzer used this method to treat a number of other patients with itching eruptions, with good results He was of the opinion that the relief of pruritus was greatest in patients with poison oak dermatitis

This report is based on the results obtained in treating nearly 100 patients with various types of itching dermatoses About 25 received treatment by the syringe method In this group were included patients with various pruritic localized and generalized dermatoses, including poison oak dermatitis and other forms of contact dermatitis, eczema (disseminated neurodermatitis), exfoliative dermatitis and localized eczemas of the hands Immediate relief of itching was noted in all cases Occasionally there was little effect from the first injection but subsequent doses resulted in prompt cessation of the itching The relief lasted for from thirty minutes to twelve hours, the average complete freedom from itching being about four hours The recurrence of itching was seldom as severe as the preceding pruritus No more than two injections were given in any twenty-four hour period The objective cutaneous lesions responded much more rapidly once the physical and psychologic trauma of itching was relieved by this treatment

Itching usually stops after the injection of 2 to 5 cc of the solution However, the full 20 cc is administered The dramatic suddenness of the relief makes a profound impression on both the patient and the physician

The necessity for repeated injections and the possible complications to be discussed later make this agent more valuable against acute pruritus than against chronic types

## DANGERS

It would be foolhardy for any one to adopt this method without knowledge of the dangers involved Carr<sup>4</sup> in 1940 mentioned a total of 55 cases from the literature and from his own experience in which this manner of treatment was used without difficulty Sperling, Weisman and Papermaster<sup>5</sup> used this drug in 169 cases following operations on

3 Kruetzer, W Personal communication to the author

4 Carr, H A Treatment of Acute Attacks of Bronchial Asthma by the Intravenous Injection of Aminophyllin, *J Lab & Clin Med* **25** 1295 (Sept) 1940

5 Sperling, L, Weisman, S J, and Papermaster, R Effect of Intravenous Theophylline with Ethylene Diamine (Aminophylline) upon Rate and Depth of Respiration, *Surgery* **11** 600 (April) 1942

the abdomen without serious ill effects. Brown and Blanton<sup>6</sup> added 31 more cases of asthma treated with the same results. Unger<sup>7</sup> stated that he had treated hundreds of patients without difficulty. My results have been the same.

On the other hand, Luduena<sup>8</sup> as the result of animal experimentation, came to the conclusion that theophylline ethylenediamine given intravenously might lead to meningeal and/or renal changes and therefore its administration should not be continued indefinitely. He did state, however, that he knew of a patient who had received two hundred injections of this drug over a period of two or three months without demonstrable difficulty.

Merrill<sup>9</sup> reported death occurring in 3 cases while the injection of theophylline ethylenediamine was being given. While all these patients showed evidence of serious heart disease, the fact that fatalities occurred while the injection was being given leaves no doubt that the drug was responsible for the deaths. Merrill mentioned 2 other deaths that he had heard of informally. I have been told of 2 other cases similar to the 3 reported by Merrill.

#### OTHER METHODS OF ADMINISTRATION

Theophylline ethylenediamine is ineffective as an antipruritic agent when administered orally, rectally or locally. The results have been somewhat beneficial when the drug was injected intramuscularly in doses of 0.5 Gm. in 2 cc. of fluid. Many patients experience relief of itching within thirty minutes, and this may persist for from hours to days, usually one to twelve hours. However, other patients fail to experience any benefit from the injection. Many patients also complain of numbness in the hip and/or the leg after the injection.

The incorporation of the 20 cc. ampule of the drug in 1,000 cc. of 5 per cent or 10 per cent dextrose decreases the toxicity. Unfortunately, the relief of itching is neither so dramatic nor so uniform as with the syringe method. In fact, 1 patient with pruritus ani suffered a severe paroxysm of itching after 600 of the 1,000 cc. of the solution had been administered by gravity.

Both the intramuscular and the gravity intravenous injections eliminate the immediate disconcerting symptoms. However, this is of little basic importance.

6. Brown, A. G. III and Blanton, W. B. Therapeutic Effects of Aminophyllin in Asthma. *South M. J.* **33**: 1184 (Nov.) 1940.

7. Unger, L. Aminophylline Deaths. *J. A. M. A.* **124**: 320 (Jan. 29) 1944.

8. Luduena, F. P. Bronchial Antispasmodic Actions of Theophylline Derivatives. *J. Pharmacol. & Exper. Therap.* **75**: 316 (Aug.) 1942.

## COMMENT

Sperling and his co-workers<sup>5</sup> demonstrated that the intravenous injection of theophylline ethylenediamine by the syringe method increases the depth of respiration by 51 per cent while the rate is 26 per cent faster after its administration. Unger<sup>7</sup> pointed out that the deaths occurred in patients with impaired cardiac reserve. These two facts possibly explain the mechanism of death. It is suggested that a patient whose cardiac condition is such that he cannot tolerate severe over-exertion should not be given the drug intravenously.

It should be remembered that patients do not die from itching. While pruritus may be nerve racking, a drug with fatal potentialities should be used with great caution to alleviate this condition. Enthusiasm for the results must not obscure the dangers. Careful selection of cases is essential.

It is of interest to note the rapid healing that occurs when the itching is relieved.

This is merely a preliminary report to acquaint other clinicians with the dramatic possibilities of this drug. Further studies are being conducted in an effort to find a safer effective way in which to administer it.

## SUMMARY

Theophylline ethylenediamine given intravenously by the syringe method in doses of 0.5 Gm proved to be an effective antipruritic agent for various dermatoses. The relief occurred immediately and lasted for from thirty minutes to twelve hours.

The results of intramuscular and gravity intravenous injection of the drug were less dramatic and less constant.

There is a definite danger of death occurring in patients with impaired cardiac reserve who are given this drug intravenously by the syringe method.

Further studies are being conducted to find a safer effective route of administration.

## BLUE NEVUS OF JADASSOHN AND TIÈCHE

Report of a Case

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THE following case of blue nevus is reported because of the unusual size of the nevus, its rapid growth and clinical characteristics of a melanoma.

A blue nevus<sup>1</sup> resembles a melanoma but it is bluish gray or blue-black, round or oval and slightly elevated. It is firm to palpation and is most frequently situated on the face or on the extensor surfaces of the extremities. It is usually benign but occasionally undergoes sarcomatous changes. Clinically, the blue nevus of Jadassohn and Tieche may easily be confused with benign pigmented nevus, pigmented basal cell epithelioma and melanoma.

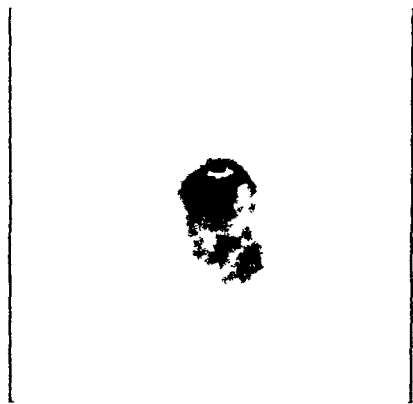


Fig. 1—Blue nevus of Jadassohn and Tieche showing features indistinguishable from melanoma. Note the unusual size.

### REPORT OF CASE

*History*—H. M., an American housewife aged 40, complained of a rapidly growing black mass on the left shoulder. She stated that she remembered always having a small wart in the brassiere strap area on the left shoulder. In the last six months, this had rapidly grown to the dimensions seen when she presented herself. Examination showed two elevated circumscribed lesions about 1/2 inch (0.96 cm) in diameter situated on a dark base. The lesions were hard and bluish black. There were no subjective symptoms. The lesions clinically resembled a melanoma (fig. 1).

<sup>1</sup> Farred, E. L. The Cutaneous Melanomas. *Arch. Derm. & Syph.* 26:110 (July) 1932.

The entire lesion was excised by the cutting current, and the base was thoroughly desiccated. As there was a remote possibility that the lesions might become malignant, the area was given roentgen ray therapy with 600 r, unfiltered, twice weekly for three weeks.

*Biopsy Report* (Dr. Fred Weidman)—The portion of the specimen selected for histologic study came from a part of the lesion which was only superficially



Fig. 2—Section from blue nevus showing close resemblance to melanoma. Pigmented cells extend from the base of the ulcer to the level of the sweat glands.

ulcerated. The epidermis was highly acanthotic in all its parts except at the site of the superficial ulceration. There was not the slightest evidence of malignant change in it. The basement membrane was closely scrutinized for the presence of Langerhans cells, but none were found. Accordingly, the pigmented lesion in the corium scarcely could be a dermoepidermal nevus.

In the center of the section there was a fairly well delimited region of pigmented tissue. It extended from the base of the ulcer almost to the level of the sweat glands but did not attain the plane of surgical excision. Within this region the collagenous bundles were widely separated by smaller and larger masses of a pigmented "tumor." The tumor had a matrix that was only slightly vascular but loosely fibrillar. On it there were great numbers of cells laden with melanin.



The pigmented cells did not have the characters of those of malignant melanoma or of a dermoepidermal nevus. In the first place, although the shape of the cells varied from spindle to polyhedral, they were relatively uniform in size. Too, they were remarkably uniformly and invariably crowded with the pigment granules—something that is inconsistent with malignant melanoma. Again, the nucleus was invariably round and relatively small. There was not any of the clustering of cells that occurs in malignant melanoma. All of these features are compatible with those of the blue nevus.

#### HISTOLOGIC SUMMARY

The patient presented a remarkably large, highly projecting and ulcerated example of a blue nevus. There is not the slightest difficulty in vetoing a diagnosis of a dermoepidermal nevus which has undergone malignancy. The possibility has been considered whether the exceptional clinical features could be explained on the basis of malignant transformation of a blue nevus, exceptional though it is. The sections do not permit this assumption, at no place were the nuclei of the character to allow that idea to be entertained. In short, the lesion could be nothing but a blue nevus in spite of its most exceptional clinical features.

#### COMMENT

A woman had an unusually large blue nevus of Jadassohn which clinically resembled a melanoma. The microscopic examination of the lesion was paramount to a diagnosis as all of these lesions present certain common characteristics and similarities.

500 Central Medical Building

## Obituaries

ALFRED POTTER, M D

1880-1945

Alfred Potter a graduate of the Long Island College Hospital in 1902, died on Dec 27, 1945, after a brief illness, at the age of 65. His medical career had been long and active. After graduation he interned



ALFRED POTTER, M D

1880-1945

at the Long Island College Hospital for two years and followed this with postgraduate training in dermatology at Columbia University as well as in bacteriology and in syphilology at the Rockefeller Institute. In his

early days of practice he was a diagnostician in the Department of Contagious Diseases, for the Department of Health, New York City. He resigned this position in 1913 to devote himself entirely to the practice of dermatology and syphilology in Brooklyn.

He served his alma mater well for many years, first as instructor in dermatology and then as professor of dermatology from 1920 to 1930. In the latter year he became emeritus professor of dermatology.

He had been honored with appointments to the dermatologic staffs of many hospitals, either as an attending physician or as a consultant. Among them were the Long Island College Hospital, Jewish Hospital, Harbor Hospital, House of St. Giles for Cripples, Bikur Cholim Hospital, Swedish Hospital, Samaritan Hospital, Home for Destitute Children, Brooklyn Eye and Ear Hospital, Norwegian Lutheran Deaconesses' Home and Hospital and Lutheran, Mary Immaculate, Jamaica, Brooklyn State and Englewood (N. J.) Hospitals. At the Kings County Hospital he served continuously from 1908 as attending dermatologist and syphilologist until 1941, when he became consultant to this service. He was the director of this department from 1923 until 1941.

Dr. Potter was a member of the Kings County Medical Society, American Medical Association, Brooklyn Medical Association, Associated Physicians of Long Island and the Hospital Graduates Club. He was also a member of Montauk Lodge 268 Free and Accepted Masons. He had been a member of the New York Dermatological Society and the Tenth International Congress of Dermatology and Syphilology. He was certified by the American Board of Dermatology and Syphilology in the founders group.

His contributions to dermatologic literature were published in *The Journal of the American Medical Association*, *Journal of Cutaneous Diseases*, *Long Island Medical Journal* and the *International Journal of Surgery*.

He was a lover of the outdoors, particularly of the sea, and spent much of his time golfing, walking and swimming. During recent years he established his summer home at Guilford, Conn.

Surviving him are his wife, Beatrice, a daughter, Mrs. John Taylor, a brother, Henry A. Potter, and two sisters, Mrs. J. R. Carpenter and Mrs. George Bailey.

E. ALMORE GALVIN, M.D.

## HARRY BAILEY, M D

1898-1946

Dr Bailey was born in New Haven, Conn, Aug 10 1898, the son of Charles and Fanny Schwartz Bailey. He attended New Haven public schools and was graduated from Yale University in 1919 and from the University of Maryland School of Medicine and College of Physicians and Surgeons in 1922. He interned at St Francis' Hospital, Hartford Conn, and did graduate work in dermatology at the New York Post-Graduate Medical School and Hospital, 1930 to 1931.

He was a member of the Yale Naval Medical Unit and a veteran of World War I.

He was chief of the dermatologic service at Mount Sinai Hospital and at Municipal Hospitals, Hartford, and was a member of the executive board of both hospitals. He was also chief of dermatology at the Hartford Dispensary. He was a fellow of the American Academy of Dermatology and Syphilology, the American Medical Association, the Hartford Medical Society and of the New England Dermatological Society. He was a former chairman of the dermatologic section of the Connecticut State Medical Society and was a specialist certified by the American Board of Dermatology and Syphilology, Inc.

He was also a member of Temple Beth Israel, the Masons, the American Jewish Congress and the Zionist Organization of America.

Dr Bailey died on Jan 12, 1946 rather suddenly after a short illness prior to which he had been in excellent health. Besides his parents who live in New Haven, he leaves his wife, the former Eva Waxman whom he married in 1932, a daughter, Susan Gail Bailey, a sister, Mrs Ernest Gladstone, of New York city, and a brother, Manning Bailey, of New Haven.

Dr Bailey gave generously of his services, often sacrificing his health and personal pleasures for the welfare of his patients. He was highly esteemed and loved by his patients, friends and associates. His willingness to aid at all times, his conservative, sound judgment, his conscientious thoroughness and his genial nature will well be remembered and missed by all who knew him.

E M S

## Correspondence

### TYROTHRICIN IN CUTANEOUS INFECTIONS

*To the Editor* —Dr Harold E. Anderson published a paper (Tyrothricin in Cutaneous Infections, *ARCH DERMAT & SYPH* 53:20 [Jan] 1946) containing serious technical mistakes which have led him to erroneous deductions. In addition, he makes assumptions which are not justifiable. The method he used in testing the activity of tyrothricin in the ointment bases was ill chosen. His results only confirm the well known fact that tyrothricin is insoluble in isotonic solution of sodium chloride and do not show that tyrothricin is inactivated by the ointments. Substances of macroscopic size, which are completely insoluble in water, simply do not diffuse through agar. If Dr Anderson had used any of the following applicable methods with the cetyl alcohol formula, he would have found full activity of the tyrothricin: (1) microscopic checking of growth or viable counts of susceptible organisms inoculated into serial dilutions of the tyrothricin ointment in fluid thioglycollate medium or broth (Difco brain-heart) with or without added serum or bovine albumin, (2) dilution of the ointment with serum or albumin agar in Petri dishes and streaking with susceptible organisms, (3) mouse protection test with *Pneumococcus* type I. In a personal communication Dr Dubos has said this *in vivo* method is the most reliable one for the assaying of gramicidin or tyrothricin.

Further Dr Anderson suggests that the components of tyrothricin react with the ingredients of the ointment bases, leading to inactivation. Such a reaction is not consonant with the nature of these substances. It is partially at variance with previously published data (Dubos, R. I. and Hotchkiss, R. D. Origin, Nature and Properties of Gramicidin and Tyrocidine, *Tr. & Stud. Coll. Physicians*, Philadelphia 10:11-19 [April] 1942). Our unpublished work indicates that the apparent reduction of the activity of tyrothricin in the presence of rats' fatty acid esters, etc. is a matter of solubility. Tyrothricin is more soluble in these substances than in water.

E. I. FORRY, M.D. and S. W. LEE, PH.D. Princeton, N. J.

# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

A STUDY OF THE TYPES OF HYPERSENSITIVITY INDUCED BY PENICILLIN ADOLPH ROSTENBERG JR and HENRY WELCH, *Am J M Sc* **210** 158 (Aug) 1945

After finding an instance of hypersensitivity of the tuberculin type to crystalline penicillin sodium in a person who had had no previous contact with this drug, the authors made a study to determine the incidence of this type of sensitivity. It was found that 5 per cent of 144 persons tested with crystalline penicillin sodium exhibited a positive reaction of the tuberculin type despite the fact that none had had any prior contact with penicillin. It was postulated that there had been previous ingestion or inhalation of spores of *Penicillium*.

Rostenberg and Welch showed that the reactions obtained following intradermal injection of penicillin sodium fall into two categories. In the spontaneously sensitive persons all reactions were of the tuberculin type. In the persons originally without sensitivity but who became hypersensitive after repeated intradermal injections of penicillin sodium, the reactions, although eventually developing into a tuberculin type of hypersensitivity, were transiently wheal-like before this stage was reached.

OSTEOMYELITIS CAUSED BY GRANULOMA INGUINALE. REPORT OF A CASE WITH CULTIVATION OF THE DONOVAN BODY IN THE YOLK SAC OF THE DEVELOPING CHICK EMBRIO. WAITER H. SHELDON, BEN R. THEBAUT, ALBERT HEYMAN and MARGARET J. WAIL, *Am J M Sc* **210** 237 (Aug) 1945

Skeletal or visceral manifestations of granuloma inguinale have rarely been noted. In the case reported by Sheldon and his associates there were characteristic cutaneous lesions, one on the penis and a larger one on the leg, which surrounded an ulcer which extended into the medullary cavity of the tibia. Donovan bodies were found in histologic sections from this case and were cultivated in the yolk sac of developing chick embryos. Since the patient stated that the ulcer appeared on the leg nine weeks before the appearance of the penile lesion, the authors concluded that the ulcer on the leg might represent a primary extragenital lesion with secondary contact infection of the penis or that the lesion on the penis was present at the same time as the ulcer on the leg, but was too small to be noticed by the patient.

GENERAL ACQUIRED ANHIDROSIS. HUGO T. ENGELHARDT and J. P. MELVIN JR., *Am J M Sc* **210** 323 (Sept) 1945

Engelhardt and Melvin state that acquired anhidrosis is even rarer than congenital ectodermal dysplasia without ability to sweat. They report a case in which a patient with general acquired anhidrosis is described. Various diagnostic procedures verified this diagnosis. Histopathologic examination of sections of skin revealed generalized atrophy of the sweat glands. With experimental modification of temperature and humidity the authors were unable to induce sweating in their patient, being able to collect only a small amount of fluid, which they regarded as resulting from simple diffusion.

DIFFERENTIAL ROLES OF LAYERS OF HUMAN EPIGASTRIC SKIN ON DIFFUSION RATE OF WATER. TRAVIS WINSOR and GEORGE E. BURCH, *Arch Int Med* **74** 428 (Dec) 1944

RATE OF INSENSIBLE PERSPIRATION (DIFFUSION OF WATER) LOCALLY THROUGH LIVING AND THROUGH DEAD HUMAN SKIN. GEORGE E. BURCH and TRAVIS WINSOR, *ibid* **74** 437 (Dec) 1944

The rates of diffusion of water through living and through dead human skin were measured in an attempt to determine the portion of the skin mainly responsible

for inhibiting diffusion and preventing excessive loss of water from the body Winsor and Burch found that the corium is the most important layer of the skin in inhibiting the diffusion of water They noted that the rate of diffusion of water through dead and through living skin is virtually the same It is noted that most observers of insensible perspiration have failed to distinguish between the part of water lost insensibly through secretions of the sweat glands and that part lost through diffusion Burch and Winsor conclude that the water that escapes through the skin of a subject resting quietly in a comfortable environment is water that has diffused through the skin and not water that is secreted by the underlying sweat glands It is suggested that the terms "insensible perspiration" and "sensible perspiration" are not specific enough and that the terms "diffusion water" and "sweat" should be employed

#### HISTOPLASMOSIS IN MAN ROBERT J PARSONS and C J D ZARAFONETIS, Arch Int Med 75 1 (Jan) 1945

Histoplasmosis for many years was believed to be a rare tropical disease, but during the past decade the disease has been found widespread in the United States and in widely scattered places throughout the world Darling characterized the disease as one in which there are irregular fever, emaciation and splenomegaly Small encapsulated organisms resembling Leishman-Donovan bodies can be found in the tissues, particularly in the cells of the reticuloendothelial system

Parsons and Zarafonitis review 56 cases of histoplasmosis which have been mentioned or described in the literature and 15 cases which at the time of this review had not yet been published They state that of the 61 cases on which there were sufficient data for analysis, some form of cutaneous lesions were present in 19 (ulcers in 9, a papular eruption in 4 and purpura, usually occurring in the last two or three days of life, in 6) Petechial hemorrhages and bullous lesions were each noted once Chronic ulcers sometimes occur in the center of the papular lesions The ulcers are frequently deep with sharp, steep edges giving a punched-out appearance Of the 15 cases which they add to the literature only 3 presented neither oral nor cutaneous manifestations In 3 there was ulceration of the tongue, 1 presented ulceration of the mouth and palate, in another there were granulomatous lesions of the mouth, lip and nose and in another there were oral granulomatous lesions and also a nodule in one auditory canal There was also 1 instance of a generalized papular eruption which may have been due to concomitant Hodgkin's disease

#### TWO CASES OF MORVAN'S SYNDROME OF UNCERTAIN CAUSE HARRY PARKS and O S STAPLES, Arch Int Med 75 75 (Feb) 1945

In 1893 Morvan first described 7 cases of painless infections of the hand He recognized the association with disease of the spinal cord which in most subsequent cases has been proved to be due to syringomyelia with trophic lesions an outstanding feature Parks and Staples describe 2 cases in which the diagnosis of syringomyelia seems improbable the fundamental disease apparently being an unusual neuropathy of undetermined origin They state that the first symptoms are sensory and usually consist of absence of pain with burns or other injuries Later there develops loss of the sensation of pain temperature and usually touch in the distal parts of all four extremities Trophic changes soon become prominent in the form of ulcers, atrophy of the bones and changes in the nails Spontaneous amputation of small parts becomes necessary by reason of infection The course of the disease appears to be relatively long The authors contrast the clinical changes with those of syringomyelia, and conclude that it is a rare disease which warrants further study

#### FATAL PANICULITIS NATHAN P FRIEDMAN, Arch Path 39 42 (Jan) 1945

Although a number of cases of a rather nonspecific type of panniculitis have been reported, reports of fatal cases are rare The following case is reported. The patient

died of staphylococcic septicopyemia and not of panniculitis as such. The ulceration of subcutaneous nodules which occurred in the case is not usually present in panniculitis, but this feature has been described in an occasional report.

LYNCH, St. Paul

MANAGEMENT OF CHANCROID IN A TROPICAL THEATER E. M. SATULSKY,  
J. A. M. A. **127** 259 (Feb. 3) 1945

The diagnosis in 1,555 cases of chancroid was made on clinical grounds alone after laboratory procedures were used to eliminate complicating diseases, particularly syphilis. The best criterion in the differential diagnosis of chancroid remains the clinical appearance of the lesions. The cutaneous reactions are at best of confirmatory value and do not alone suffice to establish a diagnosis. In cases in which there were soft, fluctuant, suppurative inguinal lymph nodes incisions and drainages were not performed. The pus was aspirated with a syringe through a cannula. After all the pus was evacuated, 1 to 15 cc. of 7 per cent tincture of iodine was instilled into the cavity. Sulfathiazole was found to be the most efficacious drug to be administered orally. One gram (15 grains) was given four times a day for five days, followed by 0.5 Gm. (7½ grains) four times a day for ten days. The average hospitalization in all cases was 11.2 days.

BLOOD AND SPINAL FLUID TESTS FOR SYPHILIS IN MALARIAL PATIENTS  
HAROLD W. POTTER, LEWIS H. BRONSTEIN and CHARLES M. GRUBER,  
J. A. M. A. **127** 699 (March 24) 1945

One hundred consecutive patients hospitalized for malaria had blood and spinal fluid taken within forty-eight hours of entrance to the hospital. These patients had no history of syphilis. The Wassermann reaction of the spinal fluid was negative in every case. Twelve per cent of the men had positive blood reactions, and an additional 10 per cent had doubtful reactions. It appears that the factors which produce the biologic false result in the blood are not present in the spinal fluid. All patients had had at least one test for syphilis on entry into the army. Physicians should be wary of making the diagnosis of syphilis from only one test in a patient who has had malaria. The authors confirmed the observation of Moore, Eagle and Mohr that serums that are positive with less sensitive tests and negative with more sensitive ones are probably not syphilitic.

BULLOUS DERMATITIS (DERMATITIS MEDICAMENTOSA) FROM PENICILLIN GEORGE  
E. MORRIS and JOHN G. DOWNING, J. A. M. A. **127** 711 (March 24) 1945

A man received 1,000,000 units of penicillin for a postoperative infection. Four days after the last injection the patient noted itching of the left hand and arm, and twenty-four hours later erythema and edema of the left hand, arm and left side of the body appeared. On the sixth day after penicillin had been injected there was tense pitting edema of the entire hand and forearm. These parts also showed erythema and multiple ruptured and unruptured bullae, filled with clear, thin, yellow fluid.

EPIDERMAL AND DERMAL SENSITIZATION EXISTING IN THE SAME INDIVIDUAL  
HARRY J. TEMPLETON, J. A. M. A. **127** 908 (April 7) 1945

Cases of epidermal and dermal sensitization from drugs, plants, foods and autogenous products are reported. Combined epidermal and dermal sensitization may occur from allergens reaching the skin from without or from within. Primary sensitization has nearly always occurred from allergens applied to the surface of the epidermis. The dermis may be sensitized to exogenous materials that have penetrated unchanged through the epidermis to reach the deeper layers, or the dermis may be sensitized to inflammatory products formed in the epidermis consisting of a union of the offending externally applied allergen and the tissue protein.



of the epidermal cells. The most frequent of these combined sensitizations are those resulting from topical application of drugs, particularly the sulfonamide compounds.

CONTROL OF SYPHILIS IN PREGNANT WOMEN UNDER THE CARE OF THE GENERAL PRACTITIONER. HERMAN M. SOLOWAY, J. A. M. A. **129** 500 (Oct. 13) 1945

The plan of treatment of pregnant women provided for a weekly intramuscular injection of heavy metal without interruption throughout the term of pregnancy and eight to ten weekly injections of an arsenical drug with an occasional rest period of four weeks. The scheme of treatment was so arranged that the arsenical drug was administered in the last weeks of pregnancy. There were normal nonsyphilitic children in 94.31 per cent of the 550 cases in which treatment was started before the end of the fourth month of pregnancy. In 83.58 per cent of the 134 cases in which treatment was begun before the end of the fifth month of pregnancy there were normal nonsyphilitic children. In 409 cases of syphilitic pregnant women placed under treatment after the fifth month, 50.6 per cent terminated in the birth of normal nonsyphilitic children. In 355 cases of syphilitic pregnant women in which no treatment was given, 26.48 per cent terminated in the birth of normal nonsyphilitic children.

THE TREATMENT OF CARDIOVASCULAR SYPHILIS WITH PENICILLIN. RALPH F. DOLKART and GEORGE X. SCHWIMMELIN, J. A. M. A. **129** 515 (Oct. 13) 1945

It was necessary to discontinue penicillin therapy for 2 patients with syphilitic aortitis because of the untoward effects noted. It has been shown that there is a rapid involution of syphilitic lesions with penicillin therapy. When cardiovascular syphilis is treated by intensive methods, frequently a therapeutic paradox occurs.

HINSCH, Denver

STUDIES ON LYMPHOGRANULOMA VENEREUM. HELEN JONES, GEOFFREY RANK and BALPAPA STIARNS, J. Infect. Dis. **76** 55 (Jan-Feb) 1945

The authors found that at blood levels of 14 to 58 mg. per hundred cubic centimeters, sulfadiazine, sulfaguanidine and sulfathiazole are the most active, sulfanilamide less so and sulfapyridine least of all. Increasing the blood level of the drugs to a point below that which is lethally toxic does not per se decrease mortality but actually increases it, because of combined disease and toxicity. Although death is prevented by sulfonamide therapy, most of the mice used in these studies became sick. This disease may merge imperceptibly into the symptoms resulting from chronic hydrocephalus.

LYMPHADENOSIS BENIGNA CUTIS CLINICAL AND PATHOLOGICAL STUDY B. BAFVERSTEDT, *Acta dermat-venereol.*, 1943, supp 2

An attempt is made to classify and clarify the confusing situation which exists with respect to a group of tumors of the cutis and subcutis which are composed of lymphoreticular tissue and characterized by a benign course

In the past, two types of such tumors have been differentiated (1) Spiegler-Fendt sarcoid and (2) lymphocytoma Bafverstedt is of the opinion that the classification should be revised and that tumors described under these two headings constitute one entity He suggests a new term for this widened conception, "lymphadenosis benigna cutis"

On the basis of this new classification, materials from 41 cases were studied, and a review was made in respect to clinical appearance, histology, etiology, pathogenesis, differential diagnosis, treatment and prognosis of this disease

Lymphadenosis benigna cutis attacks persons of all ages and occurs two to three times more frequently in women than in men The tumors involving the cutis and adjoining parts of the subcutis are bluish red and vary in size from small nodules to tumors of the size of a closed fist and plaques several times as large as a man's palm These lesions may disappear spontaneously, sometimes leaving atrophic scars

Two forms of the disease can be distinguished (1) isolated tumors which may appear in several localized regions and (2) multiple disseminated tumefactions The former occur in persons of all ages and are most common on the face, lobes of the ears, nipples and scrotum These are slow growing and seldom recur after treatment The latter, which are comparatively rare, attack older persons and appear in several regions of the body simultaneously The tumors in this form are large and deep and have a protracted course and a tendency to recur

The tumors are made up of reticuloid and lymphocytic cells in a thin argentophile reticulum to form a lymphoreticular mass The reticuloid cells usually predominate The presence of plasma cells and swelling or proliferation of the fascicular endothelium are constant findings This is the general picture of lymphatic tissue after slight or moderate inflammation In these tumors, in addition, polymorphonuclear leukocytes are sometimes present

The disease is definitely benign There is no evidence of similar lesions in places other than the skin There is no change in the normal blood picture The only change in the hemopoietic system is a mild occasional lymphadenitis Malignant degeneration has never been demonstrated

The disease must be differentiated from leukemic or aleukemic lymphadenitis, Malignant degeneration has never been demonstrated

The cause is unknown, but the author believes that in many instances the disease is a peculiar type of reaction to irritation, which may be pruritus, trauma, an insect bite and, possibly, venous stasis It occurs occasionally in conjunction with atrophic or sclerosing processes (acrodermatitis atrophicans, scleroderma, cutaneous nodules, and others) The diagnosis, to be other than presumptive, must be made by histologic examination Examination should include smears of blood and possibly of bone marrow

The disease must be differentiated from leukemic or aleukemic lymphadenitis, Boeck's sarcoid, lupus erythematosus tumidus, round cell sarcoma and polymorphous sarcoma

Both varieties are highly sensitive to irradiation After roentgen ray therapy, the isolated tumors do not as a rule recur The multiple disseminated type does recur, and no statement can be made as to whether a complete recovery is possible For the latter type, arsenic has been administered with varying success

The prognosis as to life is good in both varieties As to recovery, it is good in the isolated form but doubtful in the multiple disseminated form

**CUTIS RHOMBOIDALIS NUCHAE** F. KOGOT, *Acta dermat-venereol* **21** 631 (Aug) 1940

In a survey of 860 peasants in the mountainous country near Travnik in Yugoslavia, 22.79 per cent had cutis rhomboidalis nuchae, of which 72.72 per cent were over 80 years of age. No cases of its occurrence were observed in persons under 23 years of age. The principal provoking factor is the repeated exposures to ultraviolet rays at an altitude of 800 to 1600 meters, with the possibility of tar acting as a sensitizing agent. The disease was almost always bilateral, in only 1 case in 196 was it unilateral. Colloid degeneration of the conjunctiva was constantly observed as an associated change. In fact, a diagnosis of cutis rhomboidalis nuchae cannot be made unless the conjunctival degeneration is present. Histologically, there are degeneration of both collagen and elastin and dilatation of the blood vessels. Cutis rhomboidalis nuchae is, in Kogot's opinion, not a precancerosis, such as farmer's or sailor's skin, but a degenerative atrophy.

**THE TREATMENT OF VITILIGO WITH INTRADERMAL ADMINISTRATION OF GOLD** K. L. YONG, *Acta dermat-venereol* **21** 657 (Nov) 1940

Nine patients with vitiligo and 1 with albinism were treated by injections of a gold compound (Iopon). The 9 with vitiligo were treated by the intradermal method, and the albino was treated by both intravenous and intradermal methods. Ultraviolet ray therapy was given to 2 patients and then discontinued when the author decided that it was superfluous. Pigmentation appeared at the site of injection in all the patients with vitiligo, irrespective of subsequent ultraviolet irradiation. The treatment of the albinism was a complete failure, disproving, according to the author, that pigmentation is due to the local deposit of gold in the injected areas. No serious side reaction developed in any of these patients, although a mild sealy dermatitis, which disappeared in one week when treatment was discontinued, appeared at the sites of injection in several patients.

The author concludes that gold somehow stimulates the exhausted melanoblasts in vitiliginous areas and could not possibly help albinos, since in them melanoblasts are totally absent.

**CONGENITAL ECTODERMAL DYSPLASIA OF THE ANHIDROTIC TYPE** O. KOHLER and J. P. CHRISTENSEN, *Acta dermat-venereol* **22** 1 (Feb) 1941

Congenital ectodermal dysplasia of the anhidrotic type is characterized by the absence of sweat glands, deficient dentition, poor development of the scalp hair, saddle-shaped nose, atrophic rhinitis and occasionally the absence of sebaceous and mammary glands.

A review of the literature produced 58 cases to which the authors add 2 of their own. The patients of the 2 cases described were brothers, children of a consanguineous marriage.

# Society Transactions

## BROOKLYN DERMATOLOGICAL SOCIETY

David M Davidson, M D , President

Seymour H Silvers, M D , Secretary

Oct 16, 1944

Verruca Plana Juvenilis Presented by DR E ALMORE GALVIN

R S , a white married woman aged 38, had a few small flat brownish lesions on her cheek seven years ago, after her baby was born. These lesions increased in size and number. There were no subjective symptoms. In February 1944 all warts were curetted off, and their bases were cauterized with iodine. By June all the warts had recurred.

Examination reveals many superficial, rounded and oval, brownish elevations on the forehead and cheeks, varying in size from that of a lentil to that of a lima bean.

The patient is presented for discussion as to therapy.

### DISCUSSION

DR LESSER M FRUCHTBAUM I believe that this diagnosis is open to question. The possibility of malignancy should be borne in mind, since the lesions did recur. There is one dark lesion in particular which looks malignant, and a specimen for biopsy should be taken.

DR DAVID M DAVIDSON If one were looking for some complicated diagnosis, one could think of epidermodysplasia verruciformis, but I agree with the diagnosis as presented. I have never heard of verruca plana becoming malignant. Roentgen therapy should not be used in this case.

DR MORRIS M ESTRIN I believe that these are seborrheic keratoses. They did have the suggestive color and appeared larger and softer than those ordinarily seen in cases of juvenile warts.

DR NATHAN PENSKY If this is a case of verruca plana, then roentgen therapy is to be recommended.

DR M E GOEBEL Flat warts disappear with roentgen ray therapy.

DR LESSER M FRUCHTBAUM The diagnosis suggested by Dr Estrin, seborrheic keratoses, is closest to being correct of any presented here. These warts are not flat, and they will never respond to roentgen rays. I have had a good many patients with flat warts on the face, and such warts clear after three or four exposures to roentgen rays.

DR JOEL SCHWEIG I agree with the diagnosis as presented. This disease is an outstanding therapeutic problem. It may prove recalcitrant to any form of therapy, on the other hand, it may clear up spontaneously. To illustrate this, I wish to report a case which has been under my observation. The patient, a youth of 17, was afflicted with juvenile warts on the face and hands for several years. Roentgen irradiation, electrodesiccation, injections of a bismuth preparation and arsphenamine proved of no avail, on the contrary, the disease continued to spread. As a last resort I prescribed protoiodide of mercury in the homeopathic dosage of  $\frac{1}{40}$  grain (1.62 mg) to be taken three times daily. Within fourteen days a complete clearance of the eruption occurred. Of course, I did not claim that the last remedy was responsible for the cure. It proves again that *post hoc* is not to be confused with *propter hoc*.

DR C THOMAS CHIARAMONTE I agree with Dr Schweig that in some of these cases the warts are intractable, by and large they present a rather difficult problem in treatment

DR E ALMORE GAUVAIN I appreciate the discussion of this particular case I presented this case tonight for several reasons First, I had hoped that my diagnosis might be incorrect When I first saw the patient, in February, I made sure that the lesions were flat warts On two occasions curettement was done My previous experience with this type of treatment has been entirely satisfactory I had used protoiodide of mercury and yellow mercuric oxide locally When seen in June, she had a full fledged recurrence I prescribed yellow oxide of mercury I suspected the correctness of my diagnosis because of the growth of the individual lesions I have never seen flat warts grow as large as these lesions After examining one or two of the lesions I thought of the possibility of multiple benign cystic epithelioma, but I could not follow it through Another reason for presenting her tonight was as part of psychotherapy My experience with roentgen rays has been unsatisfactory I have used as many as six doses of 75 r and have not had satisfactory results Since the diagnosis is generally agreed on, I shall try the protoiodide again

#### Malignant Melanoma Presented by DR LESSER M FRUCHTBALM

Mrs A S, aged 71, presented herself at the clinic of the Long Island College Hospital on Jan 22, 1940, with an oval lesion of one week's duration, the size of a pea, which was of a dark color and ulcerated and situated on the right leg about 4 inches (10 cm) above the ankle joint The clinical diagnosis was infected pigmented nevus or pyogenic granuloma On January 27 the lesion was removed by surgical diathermy, and the report on the section was that the lesion was a pigmented nevus or a malignant tumor The lesion healed after several months On July 6, 1942 the patient returned with a dark blue lesion of six months' duration, which appeared at the periphery of the scar of the former lesion Microscopic examination at that time showed a malignant melanoma The lesion was destroyed by desiccation On August 31 the patient again appeared, with a dark bluish raised lesion of one week's duration, the size of a small pea, at the upper pole of the old scar (the first lesion) It was removed by desiccation On March 22, 1943 there appeared a dark spot in the center of the scar of the first lesion, which was removed by desiccation On June 14 the patient returned with a few small, black lesions of three weeks' duration, located at the periphery of the old scar They were removed by desiccation The histologic examination showed that the lesion was either a pigmented nevus or a malignant neoplasm On March 27, 1944 a new bluish lesion, the size of a pea, appeared at the periphery of the former lesion This too was destroyed by desiccation On July 24, after the lesion had healed, a new pinpoint blue spot appeared at the periphery of the old scar On September 11 a large infiltrated lesion, the size of a quarter, appeared in the center of the old scar By September 25 this mass had increased in size

On October 9 physical examination showed a granulomatous mass in the center of the old scar The examination tonight shows a mass the size of a small walnut situated in the center of the old scar The tumor mass is hard and deeply infiltrated and raised above the level of the skin, it has a raw surface, is uneven and discharges a serosanguineous fluid

To summarize The initial lesion appeared about five years ago and recurred after each destruction It has not metastasized, and the patient is in good health The histologic studies of several biopsy specimens showed a malignant melanoma

#### DISCUSSION

DR E ALMORE GAUVAIN I doubt the accuracy of the histologic diagnosis I do not believe that a patient with a malignant melanoma would survive after the tumor had been tampered with I think that this lesion is a pigmented nevus If there

is a recurrence of the primary lesion, there should be a more radical excision at the secondary operation, more and more being excised and the excision being deeper and wider

DR SEYMOUR H SILVERS It is difficult to make a histologic diagnosis on the basis of a clinical examination. Clinically, the lesion is an epithelioma. I think that even a malignant melanoma may remain inactive for many years.

DR DAVID M DAVIDSON The patient is naturally too old now for radical treatment. Besides, she has enlarged lymph nodes now. However, when the diagnosis of malignant melanoma was first made the entire lesion should have been removed by a wide excision.

DR ABRAHAM WALZER This lesion should have been excised in its entirety originally. Electrodesiccation should not have been done. At the present time the patient has palpable nodes. I still think that the proper treatment, in spite of her age, would be to excise the entire area extensively.

DR LESSER M FRUCHTBAUM I presented this case for two reasons: first, because this type of lesion is rare, and second, because physicians do not generally have patients under observation over such a long period as in this case. At the time the patient first appeared, the lesion was small. I believe that I did a thorough job of excision by surgical diathermy and that there was no justification for the removal of the leg in a person of her age. When the lesion recurred one and a half years ago, it appeared at the periphery of the old scar. Apparently I should have removed more than I did at that time. Each time I performed electrodesiccation, not excision as had been done the first time, and I destroyed at least  $\frac{1}{2}$  inch (1.3 cm) of healthy tissue beyond the lesion, I felt that if I could thus control the spread of the lesion, without resorting to radical measures, that would be justifiable. What one sees tonight is a new lesion. It is a real fulminating tumor, and it does not clinically resemble a melanoma. The patient feels well and has not lost weight, and the question that still remains is what to do further—shall one amputate the leg or leave the patient alone?

#### **Circumscribed Scleroderma** Presented by DR LESSER M FRUCHTBAUM

I H, aged 12½ years, presented herself at the Unity Hospital with lesions of four years' duration on her abdomen. These lesions are large oval-shaped plaques, about 2 inches (5 cm) in diameter, symmetrically distributed on either side of the lower part of the abdomen. The lowermost lesions are white in the center, infiltrated, leathery on palpation and surrounded by a violaceous ring. The uppermost lesions are violaceous and purple and are not infiltrated. The lowermost lesions developed first. There are no subjective symptoms.

The Wassermann reaction of the blood was negative. Examination of the urine showed no abnormalities. A blood count was within normal range, and the basal metabolic rate was —15 per cent.

#### **DISCUSSION**

DR DAVID M DAVIDSON This case is interesting, inasmuch as a similar case presented last year by Dr Silvers elicited considerable discussion. Some members did not believe that soft patches like the ones the patient presented could be scleroderma, while others thought that the eruption was scleroderma but in the stage of involution. The patient presented tonight has hard and soft patches and states that the soft patches are the young lesions and all the hard patches were soft originally and only later became hard.

DR C THOMAS CHIARAMONTE Some years ago I presented before this society a patient with scleroderma without infiltration. At that time, the case provoked considerable discussion because of its lack of infiltration. This patient presents lesions which have the typical sclerodermatous changes and other lesions which are smooth. The latter lesions are slightly pale and have a bluish red, sharply

defined peripheral zone I believe that one is fortunate in seeing this eruption tonight because it links the so-called smooth scleroderma, described by Gougerot, with true scleroderma

DR LESSER M FRUCHTBAUM Most patients with scleroderma are female The ratio is 2 to 1, and in a good many cases the basal metabolic rate is lowered I have given this patient thyroid At present the lesions are circumscribed, but they tend to spread more and more

## SAN FRANCISCO DERMATOLOGICAL SOCIETY

Dr John L Fanning, *Chairman*

Dr Frances M Keddie, *Secretary-Treasurer*

Oct 20, 1944

### A Case for Diagnosis (Sarcoidosis?) Presented by DR FRANCES A TORREY

L H, a 28 year old white woman presented from the department of dermatology, University of California, was first seen in the dermatology clinic on Oct 9, 1944

At that time she had a tender subcutaneous swelling deep in the medial aspect of the right leg, which, she says, has been growing gradually for five to six years

Examination reveals a dozen or more painless subcutaneous nodules scattered over her body Many of these, she says, have been present for a long time She discovers new ones from time to time She says that her brother has similar nodules

There is a patchy hyperpigmentation on the forehead and to a lesser degree on the face, and it has been increasing for the past year

The patient has noted a feeling of increasing fatigue for the last six months

The results of the physical examination were essentially normal

The roentgenograms of the right leg revealed a mass in the right calf, with periostitis involving the cortex of the adjacent bone

### DISCUSSION

DR MERLIN T R MAYNARD, San Jose I think that one might be just as well dealing with a case of lipomatosis The diagnosis can be established only by removal of one or several of the nodes for study Lipomatosis is more probable as sarcoidosis is a rare possibility

### Tuberculosis of the Skin Presented by DR FRANCES A TORREY

E W, a 44 year old Negro woman presented from the department of dermatology, University of California, was first seen in the dermatology clinic on Sept 5, 1944

At this time she has several bean-sized subcutaneous nodules in the supraorbital and infraorbital areas of the right eye, over the area of the left antrum, one nodule in her right forearm and another nodule above the right elbow

There are crusted granulomatous lesions on the alae nasi, and the hypertrophic injected mucous membrane of the nose almost obstructs the nasal outlet on both sides

Granulomatous nodules are also present in the conjunctivas, with some mucopurulent discharge All these lesions have been present for about a year

The physical examination gave no further information

The blood and urine were essentially normal The Kolmer and Kahn reactions were negative The basal metabolic rate was +11 per cent Tuberculin tests of the skin (in dilutions of 1 1,000 and 1 10) elicited negative reactions Roentgenograms showed a normal chest Biopsy specimens of the nasal mucosa showed tuberculous granulation tissue, a nodule from the elbow showed lipomatous tissue

## DISCUSSION

DR NORMAN N EPSTEIN I think that this case has not been completely investigated. One of the nodules apparently was not of a tuberculous nature. They are in unusual locations. The one on the cheek does not suggest tuberculosis. Apparently the patient has a tuberculous process on the nose. However, histopathologic studies of one of the nodules on her face should be made.

DR MERLIN T R MAYNARD, San Jose, Calif. Since she hails from Texas, I think that it would not be a bad idea to perform a coccidioidin test and to search slides for *Coccidioides immitis*.

DR ROBERT STEWART In respect to coccidioidomycosis, of course, *Coccidioides* should be looked for in any case of granuloma. Coccidioidomycosis cannot be ruled out by performing a coccidioidin test on her. Of course, there are other observations to be reported before a definite conclusion can be made as to whether this is sarcoid or true tuberculosis. Inoculation of a guinea pig is indicated.

**Xeroderma Pigmentosum** Presented by DR FRANCIS M KEDDIE

J A B, a white woman aged 53 years, has had pigmentation of the face, neck, arms and legs since the age of 9. Numerous epitheliomas and keratoses on the arms and face have been treated by excision, cautery and roentgen rays over a number of years. The skin is dry, with pigmented macules, telangiectasia and keratoses on the exposed area.

There is no familial history of similar diseases of the skin. Her parents were not related. Two sons, aged 23 and 29, are not affected.

## DISCUSSION

DR MERLIN T R MAYNARD, San Jose I agree with the diagnosis. One fact I should like to point out is that in the resume it is said that there is no familial history of the disease. The patient, however, stated that one of her sisters has had exactly the same manifestations. She is seven years younger than the patient and has had the disease just as long as the patient has had it. I think that this helps to substantiate the diagnosis.

DR NORMAN N EPSTEIN The disease is rarely seen in a woman the age of this patient. Most of my patients have been children, and they rarely survive to this age. It seems that she has only a moderate degree of sensitivity to sunlight. I was interested to note that in xeroderma pigmentosum the epitheliomas are frequently of the basal cell type. I had the impression that they are usually of the squamous cell type. This woman, however, has had both.

DR B V A LOW-BEER (by invitation) Some of the lesions—including one under the eye, as I remember—were treated with roentgen rays. There was another, a huge lesion on the cheek, which was treated with radioactive phosphorus. The two responded equally well to the treatment. I had as a patient a young girl, sent to me by Dr Hiram Miller, with the diagnosis of xeroderma pigmentosum. She had an epithelioma under her left eye and many others all over her body. Many of the lesions were treated before she came to me. She is 20 years old and has had the disease process since the age of 5 or 6. Her father and mother are cousins. In order to study the sensitivity to various wavelengths we tried radiation with a wavelength of 2,500 angstrom units. I wish I knew what to do for this girl.

DR FRANCES A TORREY As I remember, some of the lesions were not epitheliomas, some were angiomas.

DR B V A LOW-BEER (by invitation) Yes, and some were hyperkeratoses. One was a huge ulcerating lesion which was treated with 100 kilovolt roentgen rays. I gave her about 4,500 r.

DR REES B REES The patient under discussion lacks all symptoms of photophobia, which is an almost invariable accompaniment of xeroderma pigmentosum beginning early in childhood.



NOTE—This patient later gave the following family history Her sister, at the age of 55, with brown eyes, fair skin and light freckles, has had a few tumors removed from the face, a half-brother (same father), at the age of 40, is not affected Her mother died from the results of an accident at the age of 26 Her father is alive and well at the age of 73, he has black hair and eyes Her paternal grandfather died at the age of 84, her grandmother died at the age of 20 from a cause not known, her grandmother's sister died at the age of 30 and was thought to have had a condition similar to that of this patient No information was obtained about maternal relatives

#### A Case for Diagnosis (Eczema? Simulating Leprosy) Presented by DR JOHN GRAVES

S L, a 49 year old Chinese man presented from the department of dermatology, University of California, was first seen in the dermatology clinic on Oct 11, 1944 His complaints were of induration, thickening, lichenification and pigmentation of the face and hands

April 1943 was given as the date of onset of the disease Despite much local therapy there has been little or no improvement Itching is a prominent and constant symptom

The Wassermann reaction was negative

Allergy studies are now being conducted, and the probability of a contact allergy (vegetation) is suggested by Dr Albert H Rowe A son and a daughter of the patient are said to suffer from hay fever

#### DISCUSSION

DR OTTO E L SCHMIDT One must also consider the rosy enlargement of the ulnar nerves in this patient I think that it is compatible with what one sees in leprosy The hypertrophy of the face looks unlike the chronic excoriation of eczema I think that hypertrophy of the tissues and subcutaneous tissues as well can actually be seen

DR PAUL FASAL It seems to me that the nodules on his ear lobes are suggestive of leprosy, and I think that they should be examined thoroughly

DR MERLIN T R MAYNARD, San Jose I think that the texture of the skin itself speaks against eczema Lichenoid reactions always have a rough scaly surface This man's skin is soft I could not feel any lichenification I think that it is probably a case of leprosy simulating eczema

DR FRANCES A TORREY I think that histologic examination would settle the diagnosis

DR REES B REES A further point is that the lesions are chiefly confined to the exposed areas

NOTE—Acid-fast bacilli were not found in scrapings from the nasal mucosa or in sections of tissue removed from the forehead

#### Dermal and Ocular Pemphigus Presented by DR PAUL FASAL

F B, a white man aged 65, first seen on Oct 8, 1944, presented a generalized vesicobullous eruption on the entire skin, palate, buccal mucosa, tongue, pharynx and anus His general condition was poor He gave a history of arthritis deformans of about ten years' duration His cutaneous lesions had started around his mouth several months earlier and spread gradually On Sept 10, 1943, he was admitted to the department of dermatology of the University of California Medical School, with a diagnosis of pemphigus, and he remained there until September 23

On Oct 11, 1943, internal medication with solution of potassium arsenite U S P was started, with 1 drop three times a day, this being increased every fourth day by 1 drop until 7 drops three times a day were given Then the dosage was decreased in the same way After about ten days of this medication the fresh blisters, which still formed daily, seemed to be smaller On October 25, there was

a severe eruption of large blisters on his trunk. Ten days later great improvement in his skin and general condition was noticed, and within five more weeks his skin had healed completely.

In March 1944, there was a relapse, with vesicobullous lesions all over his skin but not on the mucous membranes. Another course of solution of potassium arsenite was started. The cutaneous lesions again subsided gradually, and there has been no severe relapse since, except for occasional small blisters. Both eyes were affected when the patient was seen first. The ocular condition was diagnosed by Dr P. Dolman as pemphigus. While he was receiving arsenical medication, the patient's skin healed but his eyes became gradually worse. At present the patient's skin shows only pigmentary changes from previous lesions, both eyes are badly damaged.

#### DISCUSSION

DR NORMAN N. EPSTEIN: There is no question about the diagnosis in my mind. It seems that I have seen more benign forms of pemphigus recently in elderly people as well as in middle-aged people. I do not believe that this is because of the therapy. These patients have remissions just as if they were spontaneous and not related to therapy. One patient was given penicillin, 1,000,000 units, without any effect whatsoever on the pemphigus. I still think that vitamin D therapy seems to do something that other forms of therapy do not. It is more satisfactory in general than anything else that I have tried. This patient has done remarkably well.

DR PAUL FASAL: I did not think that in this case improvement after arsenicals was coincidental, but of course it is possible. The patient had had vitamin D before, without apparent effect.

#### Hydroa Estivale Presented by DR OTTO E. L. SCHMIDT

J. M., a 12 year old Mexican boy, presented from Stanford University School of Medicine, complains of an eruption on the face present since 1938.

The birth and development were normal. Cod liver oil by mouth caused his face to become flushed. His father has hay fever.

The eruption began on the face and the backs of the hands as papules which became vesicular during July and August each year, especially on exposure to sun. For the remainder of the year the papules persisted.

He entered the pediatrics outpatient department in August 1942. A provisional diagnosis of allergic eczema was not substantiated by extensive cutaneous tests.

Physical examination revealed a palpable thyroid gland and dermatographia. On the entire nose, malar regions and eyelids are closely grouped erythematous papules and vesicopustules. The lower lip is edematous, dry, red, scaly and fissured. A few papules are present on the backs of the hands.

On Sept. 13, 1944, biopsy of a specimen from the eyelid showed an intraepidermal vesicle filled with polymorphonuclear leukocytes and necrotic debris. In the corium was a focal round cell infiltration and some fibrosis.

The hemogram and results of examination of a timed urine specimen and of urinary porphyrin content were normal. The Wassermann reaction was negative.

There has been some recent improvement following protection from sunlight.

#### DISCUSSION

DR FRANCIS A. TORREY: I thought that the lesions were perhaps more characteristic of lupus erythematosus than of hydroa estivale. As I understand, the latter usually clears during the winter and the lesions leave decided atrophy.

DR WILLARD M. MEININGER: When the patient was first seen, he was much worse. The eruption looked a good deal more like lupus erythematosus. I had not seen him for several weeks until this evening. The improvement is most likely due to the fact that winter has just begun. Histologic examination was done to help with the diagnosis, the observations were not characteristic of lupus erythematosus.

DR OTTO E L SCHMIDT Various possibilities have been considered As I understand, many people classify hydroa estivale in two groups, depending on the presence or the absence of porphyrinuria In the cases in which there is abnormal porphyrin present, the lesions are apt to be large and leave scars In the cases without porphyrin the patients often have smaller lesions, which may persist even through the cold weather and which usually do not produce scars This type of disease disappears with the attainment of adolescence and leaves little or no trace of the former process The histopathologic structure is typical of hydroa estivale and shows epidermal vesiculation The sweat glands are not primarily involved, as is found in granulosis rubra nasi

DR MERLIN T R MAYNARD, San Jose, Calif I agree with the diagnosis I should like to say that I have known instances in which this disease persisted during the winter months At the last meeting of the American Dermatological Association in San Francisco, there were several patients who had hydroa estivale but did not have porphyrinuria These cases were typical examples of hydroa estivale The case which is presented tonight is not typical of lupus erythematosus despite the concentration of the lesions on the nose The lesions are entirely too vascular and active for lupus erythematosus The eczematous-like patches which weep and heal with scars are more typical of hydroa than of lupus erythematosus

#### Dermatitis Herpetiformis Presented by DR PAUL FASAL

A H, an 8 year old white girl, has had a generalized vesicobullous eruption for the past seven months A few vesicles appeared on the legs following a sore throat When first seen, in March 1944, her extremities were covered with vesicobullous lesions from the size of a pinpoint to that of an egg The lesions arose from a normal skin and were extremely pruritic New vesicles continued to develop until the trunk, face and scalp were covered Many of the lesions on the trunk were grouped

Her general health is good There is no history of medication prior to the onset Use of iodized salt was discontinued in March

The white blood cell count was 19,000, with an eosinophil count of 15 per cent Contents of the vesicles were sterile

Medication with sulfonamide drugs produced toxic reactions of malaise, fever, urticaria and albuminuria Solution of potassium arsenite U S P was not tolerated Acetarsona, 0.125 Gm twice daily, was taken by mouth from April to July 1944 Until September there were several relapses, characterized by the eruption of large bullae Lately there have been no large blisters, but every four to five days crops of fresh small blisters appear on the trunk, neck or extremities There have been no lesions on the visible mucous membranes

Physical examination reveals nothing abnormal save for the skin and the hypertrophic tonsils This patient was vaccinated in the fall of 1943

#### DISCUSSION

DR MERLIN T R MAYNARD, San Jose It is of particular interest to me to see this patient tonight because during the last three months I have seen 2 children with this disease In 1 it developed soon after vaccination, and she died as the result of the disease three weeks later The other child is in Children's Hospital It is worth while to take a look at her It is said that the eruption came on five weeks after a tick bite I do not know whether the tick bite had anything to do with it, but she had definite pemphigus I gave this child penicillin, and the lesions cleared completely When penicillin was stopped and sulfathiazole was given, there was a relapse She had almost universal lesions This child is likely to die also from the way the disease is going I am much interested in the relationship of vaccination in 1 case and tick bite in the other I suggest that this is a virus disease possibly of the type of foot and mouth disease, as has been suggested in the past It is suggested that since the tick is a vector of the virus causing the

disease in cattle and vaccine is the vector of a similar virus there is possible correlation between the 2 cases

DR NORMAN N EPSTEIN This case is clinically one of dermatitis herpetiformis. The lack of constitutional symptoms and the type of lesions suggest strongly dermatitis herpetiformis.

DR FRANCES A TORREY I want to report 1 case which I have been following. I was able to keep the patient fairly clear with sulfapyridine, 2 Gm a day. I had to administer this for over a year. He is now fairly well and comfortable by taking 300 mg of nicotinic acid and 15 mg of pyridoxine a day.

DR JOHN L FANNING, Sacramento I have a boy who has remained well for about a year by taking 1 Gm of sulfadiazine a day.

DR PAUL FASAL I believe that Dr Maynard's suggestion regarding smallpox vaccination in relation to the disease should be considered. I know of several cases in which the disease started in children shortly after vaccination for smallpox.

#### **Fox-Fordyce Disease** Presented by DR NORMAN N EPSTEIN

G R, a married woman aged 37, about one year ago noticed an itching eruption of the axillas and the suprapubic area. The disease has remained stationary, without relief of symptoms during this time. Menstruation began at the age of 13 and has been regular. There have been no pregnancies. Except for a general nervousness, she has had no complaints other than the pruritus.

The results of a physical examination were normal. A thorough endocrine examination by an internist, Dr Minnie Goldberg, revealed no endocrine imbalance except a mild hypothyroidism. No evidence of ovarian dysfunction was noted.

A laboratory investigation was noncontributory. Biopsy revealed dilatation of the sweat glands, with a slight inflammatory reaction around them. Because Fox-Fordyce disease has been linked with disturbed ovarian function, Dr Goldberg first gave her male sex hormone (methyl testosterone) 5 mg sublingually daily. This caused an aggravation of the symptoms. She was later given estradiol benzoate, 25 mg, by injection weekly. There has been no definite response to five such injections.

Dr Goldberg recommends that a combination of gonadotropic and estrogenic therapy be tried.

#### DISCUSSION

DR OTTO DIEDERICH, Fresno There is no question about the diagnosis. I should like to suggest the use of estradiol benzoate ointment. I have had experience with it in 2 cases, and it helped considerably.

DR NORMAN N EPSTEIN I have nothing to add, except that the patient seems to be a little better tonight than she was the last time I saw her. Perhaps the therapy is beginning to work, despite the fact that the internist was rather discouraged about it.

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## EPITHELIOMA

Report on 1,742 Treated Patients

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THE proper treatment of epithelioma of the skin is still one of the most important responsibilities of the dermatologist. Epithelioma improperly treated can be one of the most dangerous of all diseases of the skin, yet there is no cutaneous disease which responds more readily to proper therapy and yields as uniformly good results as skin cancer in its early stages<sup>1</sup>. During recent years the public has had the benefit of educational campaigns concerning cancer, and it is responding by seeking earlier consultation and treatment. The opportunity for successful treatment is therefore greater today than ever before, and the dermatologist's responsibility to the patient is likewise increased. Lack of knowledge of the specific cause of cancer makes it urgently necessary that one evaluate the results of therapeutic measures from time to time in order to determine where and how they may be improved.

The subject material of this report is drawn from the private practice of one of us (J A E) over the twenty-two year period 1919 to 1941. During this time, 2,081 patients with a diagnosis of epithelioma were seen, of these, 208 patients had lesions of mucous membranes and their cases are not included in this report, 79 patients failed to return for treatment, and 39 were referred for surgical treatment or high voltage roentgen ray therapy. The cases of patients with Bowen's disease, Paget's disease and malignant melanoma are excluded. There remain 1,742 patients with a total of 1928 epitheliomas.

This study was undertaken with several purposes in mind—namely, to analyze the clinical observations in an extensive series of cases of epithelioma seen in private practice, to evaluate the results of the therapeutic measures used, to ascertain what additional observations should in the future be noted in each case in order to make a continuous study.

Read at the Sixty-Fifth Annual Meeting of the American Dermatological Association, Inc., Chicago, June 21, 1944.

<sup>1</sup> Elliott, J A. Treatment of Skin and Mucous Membrane Cancers, South. M J 18 343 (May) 1925.

over the next twenty years more valuable, and to see what light, if any, this series of cases might shed on some of the etiologic theories

#### ETIOLOGY

While the subject of the cause of epithelioma of the skin is too large, of course, for a complete consideration in this paper we wish to discuss briefly several pertinent features on which our material has some bearing. There is considerable laboratory and clinical evidence that hereditary susceptibility and familial incidence are important factors. Warthin's study strongly suggested a recessive familial susceptibility to the development of cancer. Our records have not always been made to include complete data on this point, but these data are now recorded routinely. However, out of 633 patients who were questioned on this point 188 reported a definite family history of skin cancer and 44 more reported some other type of cancer in the family. Thus we found a total of 37 per cent in an unselected group of 633 patients with a family history positive for cancer. Many patients who at first disclaim a history of cancer find on subsequent inquiry among their relatives that there is cancer in the family tree. It is therefore wise to request such an inquiry if the patient is in doubt, for this reason we believe it probable that the number who gave no history of cancer, 63 per cent, would be materially lessened had we been able to elicit entirely accurate family histories. One of us (J. A. E.) has in a number of instances treated epitheliomas in several members of one family, sometimes in more than one generation. One family of nine children affords a good illustration. One child died at the age of 19 (not from cancer), of the eight remaining siblings, four males and one female acquired epitheliomas, in the three others, now over 50 years of age, malignant lesions have not developed so far. The mother died of carcinoma of the uterus. Similar observations have been reported by Hailey and Hailey<sup>3</sup> and others.

One long-disputed question is, "Can epithelioma arise in normal skin?" Engman<sup>4</sup> stated that he was confident that the earliest new growth of skin cancer cells is always preceded by some degenerative change in the cutis, involving the connective tissue, elastic tissue or cellular elements, and that this changed tissue environment brings about the malignant change in the epithelial cells. Pfahler<sup>5</sup> stated the belief that skin cancer is always preceded by a mole, comedo, wart, ulcer, fissure, eczema

2 Warthin, A. S. Further Study of a Cancer Family, *J. Cancer Research* **9** 299 (June) 1925

3 Hailey, Howard, and Hailey, Hugh. Treatment of Skin Cancer in Ambulatory Patients, *J. M. A. Georgia* **29** 50 (Feb.) 1940

4 Engman, M. F. External Cancer, *J. A. M. A.* **84** 103 (Jan. 10) 1925

5 Pfahler, G. E. Treatment of Cancer of the Skin with X-Ray, Radium, and Electrocoagulation and Their Special Indications, *M. J. & Rec.* **128** 261 (Sept. 19) 1928

or scar Sutton,<sup>6</sup> however, subscribed to the theory that small cancerous lesions may arise *de novo*, i. e., on previously unaltered skin and that the earlier visible sign is a circumscribed dyskeratotic lesion. According to a recent monograph of MacKee and Cipollaro,<sup>7</sup> "probably every cancer is preceded by a pathological condition which, while it cannot be called cancer nor even precancer, from the standpoint of pathology, provides a favorable soil for such development." In many of our cases, the epithelioma developed apparently from a senile keratosis, on the other hand, some lesions do develop on what appears to be normal skin. This does not preclude the possibility of preceding microscopic changes in the epidermis or the cutis any more than it would preclude the possible role of hereditary susceptibility. On the whole, our material supports the position of MacKee and Cipollaro. On the basis of a remarkable demonstration of the histogenesis of the local spread of epithelioma, Sutton<sup>8</sup> has offered the concept of somatic mutation as the starting point of a "spontaneous" epithelioma, believing that the surrounding normal cells do not become malignant by transition, but that all the neoplastic cells are the progeny of the original mutation. His evidence supports the view that each spontaneous epithelioma of the human skin behaves like a colony of cells of a new kind.

#### TYPE OF SKIN AND ROLE OF PIGMENT

There is a certain type of skin which is more fertile soil for the development of epithelioma, namely, that of the person with blond, sandy or ruddy complexion which freckles readily but does not tan, usually associated with light hair and eyes. This is another manifestation of hereditary influence, and Weller<sup>9</sup> has suggested that this constitutional type may be thought of as exhibiting in a mild degree the condition of xeroderma pigmentosum. At any rate, these patients apparently have a low actinic tolerance, and when their occupations or avocations require prolonged exposure to the sun and wind they are prone to acquire keratoses and epitheliomas. There is likewise a general impression of some standing that epitheliomas are less likely to develop in dark-skinned persons than in light-skinned persons exposed to similar conditions. MacKee and Cipollaro<sup>7</sup> stated that blonds are affected more readily than brunets and that epithelioma is commoner in the temperate zones than in the tropics. That it is exceptionally rare in American Negroes has been conclusively demonstrated by recent surveys conducted in several Southern States by

6 Sutton, R. L., Jr. Cancer of the Skin, *J. Oklahoma M. A.* **28** 364 (Oct.) 1935

7 MacKee, G. M., and Cipollaro, A. C. Cutaneous Cancer and Precancer, New York, American Journal of Cancer, 1937, pp. 4, 15, 101, 123 and 145

8 Sutton, R. L., Jr. Epithelioma of the Skin, *Arch. Dermat. & Syph.* **46** 1 (July) 1942

9 Weller, C. V., in discussion on Apperly, F. L. Sunlight, Skin Cancer and Cancer Immunity, *Am. J. Path.* **16** 651 (Sept.) 1940

the United States Public Health Service. These surveys are referred to in detail later in this paper. Unfortunately, we have no accurate information on this point among the American Indians. The question now arises "How much of the skin's protection against ultraviolet radiation is provided by the pigment itself?" In the past it was commonly assumed that the pigment acted as a filter and that as pigmentation increased susceptibility to the local injurious action of sunlight decreased proportionately. Recent studies of the absorptive powers of the various layers of the skin and of the position of the pigment indicate that in the white skin the pigment itself provides but little protection. Bachem,<sup>10</sup> using the quartz spectrograph method, demonstrated that 66 per cent of the ultraviolet rays are absorbed in the superficial layers of the epidermis and that the basal layer and the cutis each absorbs about 16 per cent. Furthermore, skins which show no evidence of pigmentation may lose their sensitivity to sunlight after frequent exposures as a result of thickening of the stratum corneum, which becomes the protecting screen for the living epidermal cells. Laurens<sup>11</sup> has outlined the mechanism as follows. In the white skin the pigment is found almost exclusively in the basal cells, migrating to the outer layers only when the skin is well tanned. Wavelengths shorter than 3,000 angstrom units are absorbed by the horny layer and outermost cells of the malpighian layer and therefore never reach the basal cell layer. Longer waves, capable of reaching the cutis, are filtered out by the increased pigment in the prickle cell and basal cell layers, this pigment thus acts as a protective screen for the dermal papillae and the corium. In the Negro skin, on the other hand, pigment not only is more abundant in the basal cell layer but is plentiful throughout the prickle cell layer and present even in the horny layer. Meischer<sup>12</sup> expressed agreement that this fact is the main reason for the Negro's low sensitivity to ultraviolet rays. Blumenthal<sup>13</sup> stated

the immediate thickening of the horny layer in fair and red-haired persons exposed to ultraviolet rays is so impressive that it overshadows the protective mechanism of the pigment. The importance, however, of the pigment is clearly indicated in the fact that the Negro's skin is ten times less sensitive to ultra-

10 Bachem, A. Ultraviolet Transparency of the Various Layers of the Human Skin, *Am J Physiol* **91** 58, 1929. Bachem, A., and Reed, C. L. The Transparency of Live and Dead Animal Tissue to Ultraviolet Light, *ibid* **90** 600, 1929. Bachem, A., and Kunz, J. Transmission of Ultraviolet Light Through Human Skin, *Arch Phys Therapy* **10** 50, 1929.

11 Laurens, H. Physiologic Effects of Radiant Energy, *Arch Phys Therapy* **23** 153 (March) 1942.

12 Blum, H. F. Photodynamic Action and Diseases Caused by Light, New York, Reinhold Publishing Corporation, 1941, pp 177, 179, 184, 187, 252, 253, 255 and 256.

13 Blumenthal, F. Paradoxical Influence of Light Rays as a Causative and as a Curative Factor in Cancer of the Skin, *Arch Dermat & Syph* **33** 1042 (June) 1936.



violet rays than the white person's skin. Pigmentation and keratinization are definitely coordinating functions of a mechanism protective against these rays.

Another observation concerning the role of pigment was made by Findlay, who found 170 cases of epithelioma in examining 1,000,000 cattle, in all but 3 instances, the lesions occurred in white areas (cited by Sutton<sup>6</sup>).

Keller and Guillaume<sup>14</sup> expressed the belief that the principal histologic change in sunburn is a degeneration of the prickle cells, this indirectly brings about thickening of the stratum corneum, which, in turn, decreases the intensity of the sunburn wavelengths which reach the deeper cells and thereby decreases the sensitivity of the skin to sunlight. Other studies indicate that the principal absorption of sunburn radiation by the epidermis is probably due to its proteins, benzenoid amino acid structures in particular.

#### CARCINOGENIC EFFECT OF ULTRAVIOLET RAYS

That prolonged exposure to sunshine might precipitate the development of skin cancers was first suggested by Unna. In a recent monograph, Blum<sup>12</sup> has credited the first experimental production of skin cancer by ultraviolet irradiation of laboratory animals to Findlay in 1928. This work has been confirmed by many other investigators, and there is now sufficient experimental and clinical evidence to indicate that ultraviolet rays are carcinogenic. The laboratory evidence, summarized in detail by Blum<sup>12</sup> and by Cipollaro,<sup>15</sup> proves that malignant tumors (carcinoma and sarcoma) can be produced solely by the action of ultraviolet rays, derived either from the sunlight or from a quartz mercury vapor lamp. Rusch, Kline and Bauman<sup>16</sup> recently demonstrated that the carcinogenic wavelengths lie between 2,900 and 3,341 angstrom units; these coincide in part with those wavelengths most potent in the production of erythema. In discussing this work, Laurens<sup>11</sup> stated:

Neither the intensity of the energy nor the length of the daily exposure altered the rate of the production of tumors, provided the amount of energy applied per day was the same. Intense doses for short periods daily were as effective as mild intensities applied for longer periods each day. Further, it was not necessary to irradiate the animals throughout the precancerous period. Once initiated, carcinogenesis proceeds without further exposure to radiant energy. In some instances several months elapsed between the end of irradiation and the appearance of tumors.

He expressed the belief that the ultraviolet rays do not cause cancer in themselves but produce characteristic cell changes leading to precancerous

14 Keller and Guillaume, cited by Blum<sup>12</sup>

15 Cipollaro, A. C. The Dangers of Ultraviolet Radiation, *Arch. Phys. Therapy* **21** 223 (April) 1940.

16 Rusch, H. P., Kline, B. E., and Bauman, C. A. Carcinogenesis by Ultraviolet Rays with Reference to Wavelength and Energy, *Arch. Path.* **31** 135 (Feb) 1941, quoted by Laurens<sup>11</sup>

skin lesions. Any irritation, including continually and excessively applied ultraviolet rays, can cause the precancerous change to become malignant (Blumenthal<sup>13</sup>). Sutton<sup>6</sup> stated the opinion that actinic irritation alters the process of cell division so that true "mutants" arise, which continue to reproduce but are not responsive to whatever keeps normal growth within normal bounds. (The concept of mutation of somatic cells is credited to R. C. Whitman.) Recently, Little<sup>17</sup> has offered a logical concept of the mechanism of this carcinogenesis. Citing the fact that ultraviolet rays applied to the ears of rodents damage or kill many cells while around these areas adjacent cells appear to be "stimulated," he asked

Is it not much more simple to believe that the lighter exposures to ultraviolet or other radiation may disrupt or destroy the action of growth inhibitors and thus release the basic potentialities of the formerly restricted cell? Heavier doses would then destroy not only the inhibitors but the cell itself. Such an interpretation agrees with the physical description of the effects of irradiation—makes the effects of irradiation consistently a destructive process and does not require that it first be considered a stimulant and then a destructive agent.

Other authorities believe that the effect of solar radiation is purely nonspecific, acting merely as a chronic irritant.

#### PREVALENCE OF SKIN CANCER

It is, of course, possible to attach too much significance to the results of animal experimentation in considering the problem in human beings. The more frequent occurrence of cancer on the exposed parts of the body and on the lower lip in fishermen, sailors and farmers—has been noted by many clinicians. Roffo<sup>18</sup> (Buenos Aires) reported that in 1,500 cases of epithelioma no lesions, with the exception of three which developed in old burn scars or nevi, occurred on areas of the body covered habitually by clothing. In Australia, said Molesworth,<sup>19</sup> skin carcinoma is at least five times as common as it is in Great Britain, with a similar racial stock. He attributed this difference to the greater exposure to sunlight by a major portion of Australia's population.

Additional clinical evidence concerning the relationship between exposure to solar radiation and the incidence of skin cancer in the United States is now at hand. In spite of the interest aroused by the recorded

17 Little, C. C. Parental Influence on the Incidence of Cancer, *J. A. M. A.* **125** 93 (May 13) 1944.

18 Roffo, A. H. (a) Role of Ultraviolet Rays in the Development of Cancer Provoked by the Sun, *Lancet* **1** 472 (Feb. 29) 1936, (b) Can Exposure to the Sun Produce Cancer? *J. A. M. A.* **104** 1536 (April 27) 1935, (c) Cutaneous Cancer and the Sun. A Clinical and Experimental Study, *Urol. & Cutan. Rev.* **43** 411 (June) 1939.

19 Molesworth, E. H. An Introduction to Dermatology, London, J. & A. Churchill, Ltd., 1937, cited by Cipollaro<sup>15</sup>.

increase in cancer mortality, until recently very little factual information was available regarding the incidence of cancer among the living population. The need for a careful epidemiologic investigation of cancer in representative population groups was recognized by the United States Public Health Service. Since 1938 surveys of the incidence of cancer in ten metropolitan and surrounding rural areas of the United States, based on diagnoses of cases in living patients in addition to those recorded on death certificates, have been completed, under the general direction of Harold F. Dorn.<sup>20</sup> Details of the survey methods are given in the first report<sup>20a</sup> and are therefore not repeated here. Suffice it to say that this is the first complete study of this type in the United States and deserves wide attention. The data gathered give the first definite information on the incidence of cancer among the living population in different sections of the United States. Of especial importance is the demonstration of the exceedingly high incidence of skin cancer in the Southern States. The prevalence rates (number of known cases per hundred thousand population) for the ten different sections are graphically represented in chart 1 (reproduced partially from McDowell's<sup>20f</sup> report on the Dallas-Fort Worth study). In each of the southern areas and in Denver, the skin is the commonest primary site, reaching a peak in Fort Worth and Dallas, where 46.5 per cent of all cancers in white males were primary in the skin (table 1). If to this number the cases of lip and oral cancer are added, it is found that a total of 65 per cent of all malignant tumors of the male were epitheliomas. This is in striking contrast to the findings in the Chicago<sup>20b</sup> area, where only 12.5 per cent of all cancers in white males were primary in the skin. The percentages for females are considerably lower, the combined percentage for the entire population in each area is shown in chart 2. Furthermore, when one considers that there is probably more under-reporting of the cases of cancer in the southern areas surveyed, these figures are even more impressive. Undoubtedly more cancers are untreated and more are treated by quacks and therefore

20 (a) Mountin, J. W., Dorn, H. F., and Boone, B. R. The Incidence of Cancer in Atlanta, Ga., and Surrounding Counties, *Pub. Health Rep.* **54**:1255 (July 14) 1939. (b) Dorn, H. F. Incidence of Cancer in Cook County, Ill., *ibid.* **55**:628 (April 12) 1940. (c) McDowell, A. J. Incidence of Cancer in Pittsburgh and Allegheny County, Pa., 1937, *ibid.* **55**:1419 (Aug. 9) 1940, (d) Incidence of Cancer in Detroit and Wayne County, Mich., 1937, *ibid.* **56**:703 (April 4) 1941, (e) Incidence of Cancer in New Orleans, La., 1937, *ibid.* **56**:1141 (May 30) 1941, (f) Incidence of Cancer in Dallas and Ft. Worth, Texas, and Surrounding counties, 1938, *ibid.* **57**:125 (Jan. 23) 1942. (g) Sommers, H. J. Incidence of Cancer in Birmingham and Jefferson County, Alabama, 1938, *ibid.* **57**:377 (March 13) 1942, (h) Incidence of Cancer in San Francisco and Alameda County, California, 1938, *ibid.* **57**:1566 (Oct. 16) 1942, (i) Incidence of Cancer in Philadelphia, Pa., 1938, *ibid.* **57**:1843 (Dec. 4) 1942, (j) Incidence of Cancer in Denver, Colorado, 1939, *ibid.* **57**:1971 (Dec. 25) 1942.

are not reported in the southern sections than in the larger northern cities, where more clinics are available and accessible to the general population

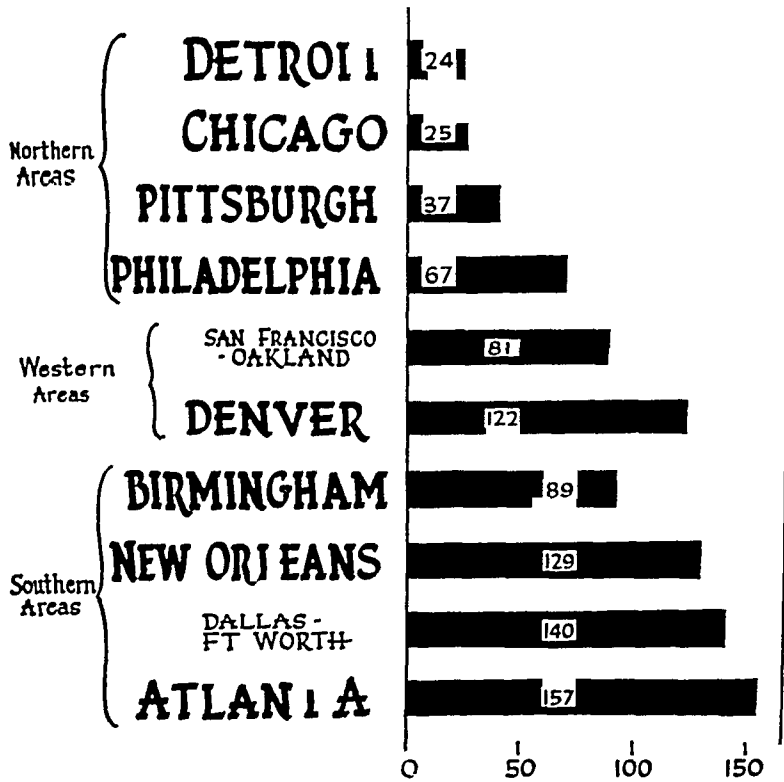


Chart 1—Prevalence rates of skin cancer (from McDowell and others<sup>20</sup>), number of cases per hundred thousand resident white population according to United States Public Health Service surveys

TABLE 1—Per Cent of all Cases of Cancer Primary in the Skin from United States Public Health Service Surveys<sup>20</sup>

	Living White Population	
	Male	Female
Dallas-Fort Worth	46.5	21.7
Birmingham	46.1	24.9
Atlanta	38.5	23.1
Denver	33.1	18.2
New Orleans	29.2	20.4
San Francisco	21.0	10.4
Philadelphia	19.8	10.7
Pittsburgh	16.0	9.0
Chicago	12.5	6.9
Detroit	12.3	6.2

Epithelioma in the southwestern states has been the subject of several reports by Phillips,<sup>21</sup> who, after moving from Virginia to Texas, was

21 Phillips, C (a) Skin Cancer in Southwest U S, read at the Third International Congress of Cancer, Atlantic City, September 1939, (b) Observations

(Footnote continued on next page)

impressed by the much higher incidence of epithelioma in the southwest. The Public Health Service survey in Dallas and Fort Worth seems to bear this out.<sup>20f</sup> They found that skin cancer accounts for one third of all cases of cancer reported in that area and occurs almost exclusively among white persons.

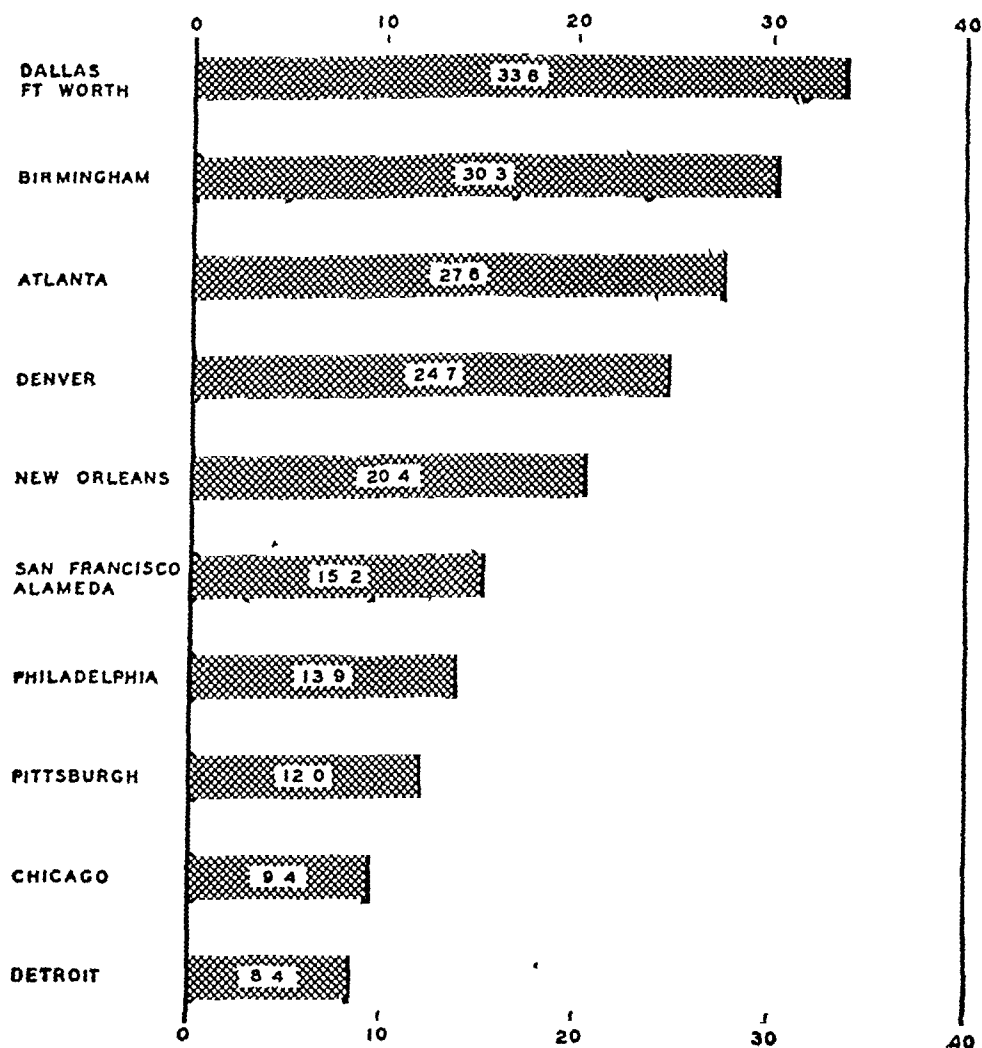


Chart 2—Percentage of all cases of cancer that were cases of skin cancer in selected urban areas, 1937-1939

#### CLIMATOLOGIC DATA

After studying the results of the Public Health Service surveys, our first thought was that the incidence of skin cancer might parallel the number of hours of sunshine in each geographic section. Through the cooperation of the United States Weather Bureau, data on this and several other climatologic factors were obtained and are shown in

Based on the Study of 1,434 Skin Cancers, *Virginia M. Monthly* 67:400 (July) 1940, (c) The Relationship Between Skin Cancer and Occupation in Texas, *Texas State J. Med.* 36:613 (Jan.) 1941, (d) Multiple Skin Cancer—A Statistical and Pathologic Study, *South M. J.* 35:583 (June) 1942

table 2 It is at once obvious that the number of hours of sunshine a year (in each section) is significant, but it is not the only factor requiring consideration For example, Dallas and Fort Worth have 30 per cent more hours of sunshine and 62 per cent more clear days than does Detroit, thus exhibiting a parallel to the prevalence rates of skin cancer in these two areas On the other hand, when New Orleans is compared with Chicago, one finds the hours of sunshine and the number of clear days almost identical, but there is a great difference in the incidence of skin cancer Note, however, that the average annual temperature is 40 per cent higher in New Orleans than in Chicago, furthermore, when one compares the average temperatures for the winter months (December

TABLE 2—*Climatologic Data, Obtained from Reports of United States Weather Bureaus*<sup>22</sup>

	U S Weather Bureau Data					Prevalence Rate Skin Cancer (White)
	Per Cent of Possible Hours of Sunshine per Year	Average Number of Clear Days per Year	Mean Annual Temperature, F	Mean Winter Temperature, F	Mean * Annual Solar Radiation	
Atlanta	60	132	61.3	46.4	379 Gainesville	157.0
Charlotte	62	132	60.2	44.6		
Dallas-Fort Worth	67	162	65.6	50.0		139.7
New Orleans	58	125	69.4	57.6	319	129.3
Denver	66	147	50.4	36.5	378 Lincoln	121.7
Birmingham	60	141	63.7	49.1		89.1
San Francisco-Oakland	66	161	56.5	52.2	391 Fresno	81.2
Philadelphia	58	114	54.4	35.9	339 Washington, D C	66.7
Pittsburgh	49	86	52.6	32.4	278	36.6
Chicago	58	117	49.2	28.9	270	25.4
Detroit	52	100	48.7	28.4		23.8

\* Where the local weather bureau station was not equipped to measure solar radiation, the reading in a nearby city is sometimes given, as indicated

January, February and March) one finds that the average for New Orleans is twice that of Chicago This, of course, means that the population of New Orleans has many more hours of exposure to sunshine than has the population of Chicago<sup>23</sup>

For a number of years measurements of solar radiation have been carried out by a limited number of stations of the United States Weather

22 Annual Meteorological Summary with Comparative Data, from Atlanta, Charlotte, New Orleans, Dallas, Chicago, Detroit, Pittsburgh, Birmingham, Denver, San Francisco, and Philadelphia, United States Weather Bureau

23 While each survey area is referred to by the name of the city, the surrounding rural counties were included in each instance, thus the statistics represent a combination of the rural data and the urban communities

Bureau The instrument used, the pyrheliometer, records the total solar and sky radiation on a horizontal surface in units of gram calories per square centimeter <sup>24</sup> This represents chiefly the caloric effect of sunshine, which is not so important in relation to skin cancer as is the ultraviolet component (Blumenthal <sup>13</sup> has pointed out that the quantum of the caloric rays is not sufficiently strong to exercise a substantial effect on the atom) No extensive measurements of the ultraviolet component are available yet, hence we have included the figures on total solar radiation for interest <sup>25</sup>

These data support the concept of an etiologic relationship between solar radiation and skin cancer It also indicates that overindulgence in solar radiation by the general public is much more dangerous than is generally realized

#### STATISTICS

Since Charlotte is within 300 miles (480 kilometers) of the Atlanta survey area and the climatic conditions of the two localities are almost identical, the data gathered by the Public Health Service survey there are particularly significant in relation to the findings in our own material The Atlanta survey, <sup>201</sup> first in the series, included Atlanta and nine adjacent Georgia counties, with a total population of 511,000 (1930), of which 308,000 were classified as urban and 203,000 rural One fourth of the total population was Negro A total of 3,200 cases of cancer (all types) was recorded and verified The most frequent site of cancer among white males was the skin in 38.5 per cent of all reported cases, among females, skin cancer accounted for 20 per cent of all cases In the Negro population, skin cancer accounted for only 2 per cent among males and 4 per cent among females The study showed further that only 6 per cent of all deaths of males and 3 per cent of deaths of females were due to skin cancer (This illustrates how misleading mortality tables may be in ascertaining the incidence of skin cancer)

The lack of a parallel between incidence and mortality is sometimes very striking In Atlanta, for example, more than 40 per cent of all deaths of males attributed to cancer were from lesions of the stomach, prostate and intestines, which comprise only 15 per cent of the lesions reported among the living The frequency of malignant lesions of the skin and of the digestive tract also offers an interesting contrast In Atlanta, 38.5 per cent of all cancers in white males were primary in the skin, in Chicago only 12.5 per cent of all cases

<sup>24</sup> Hand, I'F Review of U S Weather Bureau Solar Radiation Investigations, *Monthly Weather Rev* **65** 415 (Dec) 1937

<sup>25</sup> It is possible to calculate the theoretic amount of ultraviolet rays from these measurements, but one must take into account the smoke conditions, elevation, time of year, latitude, etc, of each station to make this accurate

of cancer were so classified. On the other hand, cancer of the digestive tract, accounting for 12.8 per cent of all cases in Atlanta, occurred in 35.2 per cent of the cases in Chicago.<sup>26</sup> The incidence of cancer of these two sites is apparently reversed in the two regions.

*Age*—The age distribution in our own cases is shown in table 3. The greatest number of cases, 27.7 per cent, occurred in the age 50 to 59 group, with the 60 to 69 group showing 25.3 per cent. Of 461 patients, Zeisler<sup>27</sup> found 123 in the 51 to 60 age group, 115 in the 61 to 70 group and 110 in the 41 to 50 group. Warren, Simmons and Rea,<sup>28</sup> reporting on 757 cases, found the median age for males to be 63 and for females 64. Phillips' <sup>21b</sup> series (1,182 patients) showed 38.5 per cent of those with basal cell lesions between ages 60 and 70, in the group with squamous cell lesions, 23.5 per cent were between 50 and 60 and also between 60 and 70. Schrek and Gates<sup>29</sup> reported a mean age of 57.3 years for patients with basal cell lesions and 66.2 years

TABLE 3—*An Analysis, by Decades, of the Ages of Our Patients*

Decade	Patients	
	Number	Per Cent
10-19	2	0.1
20-29	34	1.9
30-39	121	6.9
40-49	274	15.7
50-59	483	27.7
60-69	441	25.3
70-79	322	18.4
80-89	61	3.5
90-99	3	0.1
Total	1,754	

for those with squamous cell lesions. In the Atlanta survey 40 per cent of patients with skin cancer were 65 or over. Fifty-three per cent of our patients were between 50 and 69 years old, the total of the age group 40 to 79 is 87.1 per cent. The Public Health Service surveys also show appreciable numbers of epitheliomas in every age group above 35, the point is stressed that the prevalence of skin cancer "is directly associated with age and its relative importance increases regularly with age."<sup>20a</sup>

*Sex*—MacKee and Cipollaro<sup>7</sup> stated that only about 30 per cent of cutaneous cancers occur in women. The Public Health Service

26 Mountin, Dorn and Boone<sup>20a</sup> Dorn<sup>20b</sup>

27 Zeisler, E. P. Cancer of the Skin, Surg., Gynec. & Obst. **56** 472 (Feb., no 2A) 1933

28 Warren, S., Simmons, C. C., and Rea, S. Cutaneous Carcinoma Diagnosed Clinically Without Biopsy, J. A. M. A. **114** 1619 (April 27) 1940

29 Schrek, R., and Gates, O. Cutaneous Carcinoma, Arch. Path. **31** 411 (April) 1941



surveys show that the majority of epitheliomas occur in males, the percentage varies with the geographic section (table 1). The sex differential is even more pronounced in cases of cancer of the lip. There appears to be a definite relationship between the primary site of cancer lesions and sex as well as age. Of our 1,742 patients, 1,000 (57.4 per cent) were male and 742 (42.6 per cent) female. This ratio is almost identical with that found in the Atlanta survey of a total of 882 cases of skin cancer, 58.1 per cent of the patients were male and 41.9 per cent female. Zeisler<sup>27</sup> reported 55 per cent males in his group. Templeton<sup>30</sup> found the sexes about equally represented in his cases. Warren, Simmons and Rea<sup>28</sup> also found the numbers of males and females strikingly similar, they stated the belief that this is not a true reflection of the incidence in the two sexes but is probably due to the fact that women are more aware of lesions of the face and oftener seek treatment. After studying the relationship between sex and the histologic type of epithelioma, Lunsford and Taussig<sup>31</sup> concluded that males are two and one third times as susceptible to basal cell lesions as females and nineteen times as susceptible to squamous cell lesions.

*Occupation* We classified our patients into two main groups on the basis of their stated occupation indoor and outdoor, the tabulation showed 59.4 per cent (1,036) of the patients having an indoor occupation and 40.6 per cent (706 patients) an outdoor occupation. However, all housewives (urban and rural) were included in the indoor group because detailed information on each case was not available, likewise, many businessmen recorded as having an indoor occupation spend much of their time out of doors. It appears that if we had detailed information in each case the figures would show a higher percentage in the outdoor group. Phillips'<sup>21c</sup> tabulation of the occupations of 1,190 Texas patients with epithelioma showed that men and women having much exposure to the sun through working or living conditions had 46.05 per cent of the skin cancers. Of 256 patients with squamous cell epithelioma of the skin seen at the Mayo Clinic, Broders<sup>32</sup> found that 54 per cent were farmers. An intensive study by Stephenson and Peller<sup>33</sup> of skin cancer in the United States Navy, where a population of male adults 16 to 50 years of age is

30 Templeton, H. J. Cutaneous and Mucous Membrane Cancer, California & West Med **55** 81 (Aug) 1941

31 Lunsford, C. J., and Taussig, L. Superficial Epitheliomata, California & West Med **25** 740 (Dec) 1926

32 Broders, A. C. Squamous Cell Epithelioma of the Skin, Ann Surg **73** 141 (Feb) 1921

33 Peller, S., and Stephenson, C. S. Skin Irritation and Cancer in the U. S. Navy, Am J M Sc **194** 326 (Sept) 1937

much exposed to sun, wind and salt water, showed a morbidity seven to nine times higher and mortality three times higher than that of the comparable civilian population. We have previously noted the high incidence of skin cancer in Australia,<sup>19</sup> where a major portion of the population is exposed to solar radiation in daily life.

*Duration*—This factor is extremely difficult to determine accurately. When a patient is first asked about the duration of his lesion, he often underestimates it. Very few patients note the date on which a lesion is first noticed, and therefore an accurate estimate by them is difficult. Our data are based on the period between the day the patient recalls having first noticed the lesion and the day he came to us for treatment. Of our patients 38.6 per cent reported a duration of one to three years, 16.9 per cent of four to six months and 14.8 per cent of one to three months (table 4). In the senior author's series reported in 1924, 42 per cent were of one year to three years' dura-

TABLE 4—*Duration of 1,928 Epitheliomas (1,742 Patients)*

Duration of 1,928 Lesions	Number	Per Cent
1 - 3 months	287	14.8
4 - 6 months	327	16.9
7 - 12 months	91	4.7
1 - 3 years	749	38.6
4 - 6 years	254	13.1
7 - 10 years	112	5.8
11 - 20 years	88	4.5
20 or more years	24	1.2

The figures represent the period of time between the day the patient recalls having first noticed the lesion and the day he reported for treatment.

tion, with 30 per cent under one year. Simpson and Ellis<sup>34</sup> (500 cases) found 35 per cent of their epitheliomas of a duration under six months. This is encouraging, but certainly with additional education of the public the average time between appearance and seeking treatment should be constantly lessened. In the Public Health Service survey of Pittsburgh,<sup>20c</sup> 42 per cent of all patients with cancer reported a duration under six months, the duration of a majority of the lesions of the skin was under twelve months.

*Size of Lesions*—Our lesions were divided according to their surface diameter into three main groups: small (less than 0.5 cm.), medium (0.5 to 1 cm.) and large (over 1 cm.). Of the 1,928 lesions 45.6 per cent were small, 26.4 per cent were medium and 27.9 per cent were large. Accordingly, it is apparent that 72 per cent were 1 cm. or less in surface diameter. Warren, Simmons and Rea<sup>28</sup> likewise found two thirds of their lesions 1 cm. or less in diameter.

<sup>34</sup> Simpson, C. A., and Ellis, F. A. Some Modern Problems in Skin Cancer, *Virginia M. Monthly* 65:123 (March) 1938.

It is well known that many epitheliomas, especially the ulcerated lesions, are more extensive than the surface appearance indicates, this is a common observation when the curet is used. Warren and Lulenski<sup>35</sup> have stated that the size of the lesion is of considerable prognostic importance, they had only 9 per cent failures for lesions 1 cm in diameter or smaller, but they had 65 per cent failures for lesions over 5 cm in diameter. In our material, 50 per cent of the failures were for extensive lesions (over 5 cm). Fortunately, these large lesions are not so common as they were twenty years ago.

*Clinical Form* There are numerous clinical classifications, and, as MacKee and Cipollaro have pointed out, many of the varieties are temporary, one type changing to another over a period of time. The following clinical types and the numbers of each were recorded: 578 papules (29.4 per cent), 495 nodules and tumors (25.6 per cent), 333 superficial ulcers (17.2 per cent); 324 deep ulcers (16.8 per cent), 139 verrucous lesions (7.2 per cent), 30 cutaneous horns, degenerated base (1.5 per cent), and 29 senile keratoses, malignant base histologically (1.5 per cent). We found that ulcerated lesions accounted for 34 per cent, the largest of any group. Wilson<sup>36</sup> found the rate of ulceration more rapid in patients over 56 years of age and in previously treated lesions, in squamous cell lesions it was directly proportional to the grade of malignancy, except grade IV lesions, which were found to ulcerate at a rate between that of grades I and II. There are, accordingly, several possible factors in our findings. First, ulceration is a common characteristic of epitheliomas. Second, the age group commonest in our series was 50 to 69. Third, the patients with ulcerated lesions are probably more frightened by the appearance and therefore come for treatment.

*Location* There is general agreement that epitheliomas occur principally on the exposed portions of the body, with a considerable majority on the face. Our figures (table 5) show the greatest number, 30.2 per cent, occurring on the cheeks, with the nose the site of 27.1 per cent of all lesions. More than half of the total in these two locations, when the forehead, temples, eyelids, chin and jaw are added, the face is the locus of 77.8 per cent of all lesions in our cases. In Zeisler's<sup>27</sup> cases (461) also, the nose and cheek accounted for the largest number of lesions. Simpson and Ellis<sup>34</sup> found 95.7 per cent of their lesions on the exposed portions of the head and neck (500 cases of keratoses and epitheliomas). Similar observations have

35 Warren, S., and Lulenski, C. R. End Results of Therapy of Epithelioma of Skin, Arch Dermat & Syph **44** 37 (July) 1941.

36 Wilson, W. D. Rate of Ulceration of Epitheliomas of the Skin and Lip, Arch Dermat & Syph **41** 667 (April) 1940.

been reported by Hailey and Hailey,<sup>3</sup> Wilson,<sup>36</sup> and others. These data emphasize the importance of exposure to solar radiation as a causative factor.

*Multiple Lesions*—Of our patients, 9.6 per cent had more than one lesion when first seen, of these, 136 patients had two epitheliomas, 21 patients had three and 8 patients had four or more lesions. In addition, 9.7 per cent of all our patients subsequently had one or more additional epitheliomas (not recurrences) and returned to us for treatment. About 10 per cent of Zeisler's patients<sup>27</sup> presented multiple lesions. Phillips<sup>21d</sup> found that 226 of 1,400 patients with epitheliomas (diagnosis verified by microscopic examination) had multiple lesions (total of 704). The common findings in his group were: age 50 to 60, occupation, outdoor, complexion, 50 per cent blonds, site of elec-

TABLE 5—Location of 1,928 Epitheliomas

Location (in Order of Frequency)	Number	Per Cent
Cheek	584	30.2
Nose	523	27.1
Temple	152	7.8
Ear	122	6.3
Neck	120	6.2
Forehead	109	5.6
Eye lid (skin only)	112	5.8
Hand (dorsum)	56	2.9
Chin and jaw	46	2.3
Trunk	22	1.1
Nasolabial	30	1.5
Scalp	19	0.9
Arm	14	0.7
Leg	8	0.4
Finger	8	0.4
Genital (external)	2	0.1
Perianal	1	0.05

tion, the face. He stated the belief that three factors account for the multiplicity: (1) individual type of skin susceptible to development of epitheliomas, (2) occupational exposure to sunlight and (3) age.

*Microscopic Study*—Histologic examination of the lesions was performed in all cases in which the diagnosis was at all questionable, such as the cases of very early lesions, and all cases of extensive lesions, it was performed routinely in all cases of cancer of the lip. We feel that for the average, typical-appearing lesion the proper use of the curet is of diagnostic as well as of therapeutic value, in agreement with Pusey,<sup>37</sup> who stated: "I am willing to uphold a diagnosis of epithelioma made by inspection and with the curet." In Templeton's<sup>30</sup> series biopsy specimens were taken from about 20 per cent of the treated lesions, approximately one half were basal cell and one half squamous cell lesions. He reported a "similar biopsy

37 Pusey, W. A., in discussion on Elliott, J. A. Treatment of Epithelioma of the Lip by the Dermatologist, Arch. Dermat. & Syph. 27: 373 (March) 1933.

policy" (omitting it when the lesion is typically epitheliomatous in appearance) among a large number of leading dermatologists in this country. In our own material histologic examination was obtained in 381 cases, in 48.8 per cent the lesions were basal cell, in 41.7 per cent squamous cell and in 9.4 per cent combined basal and squamous cell. The somewhat high percentage of squamous cell lesions is probably due to the fact that this was a selected rather than a consecutive series. Warren and Lulenski<sup>35</sup> reported that 70 per cent of the lesions on which they had performed biopsy were basal cell in type. Montgomery<sup>38</sup> has stated that approximately 12 per cent of epitheliomas are of the basal cell-squamous cell variety.

*Previous Treatment* Two hundred and ten patients (12 per cent) had had previous treatment when they were first seen by us. Of these, 50 had had temporary healing and then recurrence, the remainder had not obtained even temporary healing. Sixty-nine patients, the largest single group, said they had been treated by "cancer quacks" (with pastes, acids, etc.). Of the orthodox therapeutic methods, radiation used alone (64 patients) and the "electric needle" (48 patients) were responsible for most of the unsatisfactory results. In addition, surgical excision had failed in 31 patients and solid carbon dioxide in 9. In our own group with recurrences and failures 40 per cent had had previous treatment elsewhere. This is in line with other reports to the effect that unsuccessful previous treatment, particularly radiation used alone in high dosage, increases the difficulty of any subsequent therapeutic procedure and renders the prognosis much less favorable.

#### TREATMENT

The historical background of the treatment of epithelioma has been traced by Jones and Alden,<sup>39</sup> Leslie Roberts,<sup>40</sup> Valade,<sup>41</sup> and others. The beginning of the present century saw the introduction of several valuable therapeutic measures, notably roentgen rays and radium, and more recently electrosurgical treatment has been introduced. MacKee<sup>42</sup> stated that the first basal cell epithelioma treated with roentgen rays was demonstrated before the Swedish Medical Society

38 Montgomery, H. Early Recognition and Treatment of Skin Cancer, *S Clin North America* **17** 1249 (Aug) 1937.

39 Jones, J. W., and Alden, H. W. Skin Cancer, *J M A Georgia* **19** 23 (Jan) 1930.

40 Roberts, H. L. Treatment of Rodent Ulcer by Trichloroacetic Acid, *Brit M J* **1** 794 (April 30) 1927.

41 Valade, C. K. Arsenic Paste in Cancer of the Skin, *J Michigan M Soc* **33** 513 (Sept) 1934.

42 MacKee, G. M. Basal Cell Epithelioma. Roentgen Ray and Radium in Treatment, *J Cutan Dis* **37** 179, 1919.

in 1899 by Steimbech. In the United States the first attempt to treat epithelioma with roentgen rays usually resulted in temporary disappearance or unimprovement with frequent recurrence, according to Geyser<sup>43</sup>. About this same time Sherwell<sup>44</sup> demonstrated an improved technic combining the usefulness of the curet with the chemical effects of a caustic.

Fordyce,<sup>45</sup> Culver,<sup>46</sup> MacKee<sup>42</sup> and many other authorities have advocated removal of the epitheliomatous mass by means of curettage before application of further therapy. It is obvious that the removal of the cancerous tissue allows any subsequent therapeutic measure a much greater chance for success than if it had to penetrate the epitheliomatous mass first. Curettage gives valuable information about the depth and extent of the lesions as well as supplying tissue for microscopic examination. It is now generally agreed that no one therapeutic method is best for all cases of epithelioma. The primary and most essential object of any form of treatment employed is, of course, the total and complete removal or destruction of every malignant cell present. Factors such as the size, location, extent, clinical form and cellular type should guide the clinician in his choice of a therapeutic method. Jacobson<sup>47</sup> has summarized it thus: "The successful treatment of cutaneous malignancies depends upon two essential requirements. First, the selection of the proper therapeutic agent to meet the needs of a given situation, second, skillful and adequate handling of the chosen remedial agent in every instance."

Briefly, the method we have employed most often is this: First, thorough curettage of all the abnormal tissue, followed by electrocoagulation or desiccation of the new surface, then the area thus treated, plus a peripheral margin of normal skin, is exposed to 600 to 800 r of unfiltered roentgen ray (105 kilovolts, 5 milliamperes, focal skin distance 9 inches [22.8 cm] mechanical rectification) on the same day. This exposure is repeated, preferably every four to seven days, until a total of 2,400 to 3,000 r has been given. We believe that this method of administering roentgen rays produces results superior to those obtained when the same total dose is given at one sitting. The time required for healing ranges

43 Geyser, in discussion on a Case of Epithelioma of the Eyelid, *J. Cutan. Dis.* **29** 610, 1911.

44 Sherwell, S. Further Observations on the Technique of an Efficient Procedure for the Removal and Cure of Superficial Malignant Growths, *J. Cutan. Dis.* **28** 487, 1910.

45 Fordyce, J. A., in discussion on Stelwagon, H. W. Roentgen Rays in Dermatology, *J. Cutan. Dis.* **24** 97 (March) 1906.

46 Culver, G. D. The Treatment of Epithelioma by Curetting, Followed by Cauterization with Chromic Acid and Later by Exposure to X-Rays, *California State J. Med.* **9** 340, 1911, abstracted, *J. Cutan. Dis.* **29** 649, 1911.

47 Jacobson, H. P. Actual Cautery in the Treatment of Cutaneous Cancer, *Urol. & Cutan. Rev.* **41** 871 (Dec.) 1937.

from four to seven weeks, depending on the original size and depth of the lesion

According to Brodeur,<sup>48</sup> the Brocq-Belot technic was one of the first to employ the combination of curettage and roentgen ray therapy Savatard,<sup>49</sup> in 1928, stated that for twenty five years his method of treating (basal cell) epitheliomas had been curettage followed by chemical cauterization and roentgen ray therapy Culver,<sup>46</sup> Bechet,<sup>50</sup> Shelmire and Fox,<sup>51</sup> Zeisler<sup>27</sup> and many others have reported superior results following the combined use of curettage, electrothermic or chemical cauterization and roentgen ray therapy The advantages of electrothermic methods supplemented by roentgen ray also have been pointed out by Pfahler,<sup>52</sup> Hazen,<sup>53</sup> Simpson and Anderson,<sup>54</sup> Lingenfelter and Ambler,<sup>55</sup> and others Curettage and electrothermic cauterization offer the only hope in many cases in which previous radiation therapy alone has failed

The matter of the cosmetic result is important Although some of the older authorities recommended a total disregard of cosmetic consideration, it must be conceded that, as Shelmire and Fox<sup>51</sup> have stated, "Utter disregard for the surrounding tissues in their treatment leaves as a sequel disfiguring cosmetic results often as annoying to the patient as the primary growth itself The tell-tale atrophy and telangiectasia subsequent to the overzealous treatment of a small basal-cell epithelioma with massive x-ray and radium irradiation may be not only deforming, but in itself dangerous, as not infrequently a malignant prickle-cell epithelioma develops upon the site of the radiodermatitis" Admittedly, the physician's first and foremost duty is to apply the therapeutic method which offers the greatest possibility of cure, but his obligation to the patient includes an effort to bring about a complete cure with a minimum of permanent deformity The scars incident to the use of curettage and electrothermic methods tend to improve with the passage of time, whereas the cutaneous changes induced by high dosage radiation frequently do

48 Brodeur, P Brocq-Belot's Technique in the Treatment of Superficial Skin Cancers, *Canad M A J* **49** 109 (Aug) 1943

49 Savatard, L Treatment of Cancer of the Skin, *Lancet* **1** 823 (April 21) 1928

50 Bechet, P E Diagnosis and Treatment of Cutaneous Cancer, *M Rec* **148** 50 (July 20) 1938

51 Shelmire, B, and Fox, E C Treatment of Skin Cancer, *South M J* **28** 489 (June) 1935

52 Pfahler, G E, and Bastine, J H Treatment of Epithelioma of the Skin, *Radiology* **23** 542 (Nov) 1934

53 Hazen, H H Late Results from Combined Electrocoagulation and Irradiation of Superficial Cancers, *Am J Roentgenol* **30** 806 (Dec) 1933

54 Simpson, C A, and Anderson, H F Studies and Report of Five Hundred Epitheliomas, *Virginia M Monthly* **56** 92 (May) 1929

55 Lingenfelter, G P, and Ambler, J V Early Recognition and Treatment of Malignancy of the Skin, *Colorado Med* **31** 189 (June) 1934

the opposite Those who have used the combined method of treatment generally agree that the cosmetic result obtained is equal to and frequently superior to that obtained by other methods

### RESULTS

The results obtained in 1,052 cases followed for five years or more are shown in table 6 Of these, 647 were observed personally, in 405 follow-up information was furnished by questionnaires Five year cures were obtained by 97.1 per cent of the patients The lesions of 563 patients healed satisfactorily under treatment, but the patients could not be followed up There are, in addition, 60 four year cures and 67 three year cures among patients seen since 1939 Primary healing of the lesion is no criterion of permanent cure, but in too many reports it has been considered as such Emphasizing this point, Warren, Simmons and Rea<sup>28</sup> reported that more than 25 per cent of the deaths from cutaneous cancer in their series occurred after primary healing Warren and Lulen-

TABLE 6—Results Obtained for 1,052 Patients Followed for Five Years or More

Results	Patients	
	Number	Per Cent
Patients followed five years or longer	1,052 *	
Recurrences	15	1.4
Failures, including deaths	15	1.4
Deaths	3	0.3
Five year cures	1,022	97.1

\* The remaining 563 patients had healing under treatment but could not be followed There are in addition, 127 patients with three or four year cures, seen since 1939

ski<sup>30</sup> found that 42 per cent of the recurrences developed two years or more following original healing There is still a paucity of reports on the late results obtained in the treatment of epithelioma

*Recurrences and Failures*—We had a total of 30 patients (2.9 per cent of the five year group) whose lesions recurred after our treatment or failed to heal Of this group 64 per cent were males, the average age was 61.5, and 40 per cent had been treated previously elsewhere We consider as recurrences only those lesions which healed after our treatment but later broke down, these total 15, and in all but 1 instance the recurrence developed within five years after the original treatment In 11 of these cases final cure was obtained, usually by repeating our treatment (several had been originally treated with roentgen rays alone or Sherwell's technic alone) In 4 cases the final outcome could not be learned, they are therefore added to the number of failures

In addition, the group classified as failures includes 15 with persistent lesions which never healed under our treatment In 5 of these, underlying cartilage (ear) was involved, and 4 obtained final cure fol-



lowing surgical excision, which is certainly the treatment of choice when underlying cartilage has been invaded. One patient's lesion, on the dorsum of the hand, recurred again after surgical excision and finally necessitated amputation. Seven out of the 15 had extensive lesions (over 5 cm) to start with, covering the entire temple, forehead or cheek. Six were treated continuously without healing and then lost track of, their treatments are considered as failures, but the final outcome is unknown to us.

We know of only 3 patients in whom metastases developed, and they died, there have probably been more, but our records, inquiries and questionnaires have revealed no others. It is possible that 1 or more of the cases with extensive lesions which resisted all treatment ended fatally. These factors naturally render any calculations of the percentage of failures and fatalities of limited value.

Comparison with statistics published in other reports is difficult, owing to the variety of therapeutic procedures, methods of calculation, length of follow-up, etc. Templeton's<sup>30</sup> material was in many respects similar to our own, reporting on 1,281 patients, including some with lesions of mucous membranes treated in private practice, he noted 37 recurrences and failures, including 2 deaths. Analyzing the methods of treatment employed, he found that the use of destructive forms of therapy resulted in far fewer recurrences than the use of radiation alone. Of his 1,040 cutaneous lesions 98.7 per cent were classified as cured, however, only 22 per cent of these had been followed for five years. Warren, Simmons and Rea<sup>28</sup> reported on 829 cases of epithelioma and were able to follow 84 per cent for five years. Recurrences occurred in 13 per cent of their cases with primary healing and followed for one year or longer. Their patients were treated almost exclusively by radon alone, estimated five year cures were 65.5 per cent. They attributed their failures "largely to the use of very light filtered radon applied to the surface in inadequate dosage." Their mortality rate was 0.4 per cent in cases of lesions under 1 cm in diameter, 35 per cent in cases of lesions over 4 cm. In a series of cases with microscopic verification and treated with surgical measures or radiation, Warren and Lulenski<sup>35</sup> reported 39 per cent five year cures in cases of squamous cell lesions and 41.4 per cent in cases of basal cell lesions. Mortality rates were 34.4 per cent for squamous cell lesions, 11 per cent for basal cell lesions and 5 per cent for a group of lesions on which biopsies were not done. MacKee and Cipollaro<sup>7</sup> have tabulated the results reported by a number of writers. The combined use of curettage surgical diathermy and roentgen ray treatment resulted in 94 per cent cures in Zeisler's series.

To summarize our results, Of 1,742 patients with epithelioma, 1,052 (60.3 per cent) were followed for five years or longer, of these 97.1 per cent had five year cures. Warren and co-workers<sup>28</sup> expressed the belief

that the percentage of cures should be computed on the basis of the total number of lesions treated rather than the number of patients followed, by this method we would have 58.6 per cent known five year cures out of 1,742 patients treated, 1.7 per cent recurrences and failures and 39.7 per cent of the patients unaccounted for after primary healing. In a total of 30 cases recurrence or failure to heal was known, ultimate cure was obtained in 16 of these. There were 3 known fatalities, a mortality rate of 0.3 per cent in the 1,052 cases followed five years.

#### COMMENT

The high incidence of epithelioma in the Southern States, as demonstrated by the recent United States Public Health Service surveys, not only indicates the importance of the therapeutic problem but also lends considerable additional support to the concept of an etiologic relationship between solar radiation and skin cancer. The statistical findings in our own material are very similar to those reported in the Atlanta survey and to those published in other private reports. Regarding statistics, we make a plea for a careful and complete history in each case of epithelioma. This should include, in addition to the customary data, as much information as can be gained about the family background and history of cancer, the type and color of the patient's skin, how much exposure to sunshine, wind and other irritants the patient has had in addition to that to be expected in his regular occupation, and the first sign of the lesion. Furthermore, to make possible more accurate and valuable comparisons between different reports a standard form (to include various treatment procedures, comparative data and a uniform method of computing statistics) would be of great value. To carry this idea to its logical conclusion, a central clearing house for the collection, standardization and dissemination of this material should be established.

#### SUMMARY

1. The high incidence of epithelioma in the white population of the Southern States supports the concept of an etiologic relationship between solar radiation and skin cancer and emphasizes the importance of the therapeutic problem. 2. An analysis of the clinical observations and the results obtained in the treatment of 1,742 patients with epithelioma of the skin is presented. 3. The combined use of curettage, electrothermic destruction and roentgen ray therapy resulted in 97.1 per cent cures in 1,052 patients followed for five years or longer. This has proved to be an ideal therapeutic procedure for the average epithelioma.

Mr. James M. Howe, Chief of the United States Weather Bureau at Charlotte, N. C., assisted in obtaining the climatologic data.

403 North Tryon Street

## ABSTRACT OF DISCUSSION

DR HOWARD HAILEY, Atlanta, Ga The Association is indebted to Dr Elliott for his instructive paper Apparently, from statistics cited by Dr Elliott, skin cancer is much more prevalent in the Atlanta area than in some other areas which are similar in geographic location I think that this apparent frequency can be partially explained by the fact that there are three active cancer clinics in Atlanta In addition to these three clinics, there are nine other treatment centers throughout the state of Georgia Because of the comparatively numerous cancer clinics in the state of Georgia, better statistics are available I dare say that if some of the surrounding states had as many active cancer clinics as Georgia has, the incidence of skin cancer would be much greater than now reported

For a long time it has been known that solar radiation exercises a strong influence in the development of cancer of the skin Dr Elliott has emphasized this point in an interesting and authoritative presentation Solar radiation is probably the commonest exciting factor in the development of cancer There are certain occupations in which exposure to gases, chemicals and other irritating substances offer exciting causes in the development of cancer I believe that it is necessary to have the hereditary factor present in the patient before the exciting factor—solar radiation or other factor—can bring about development of skin cancer As Dr Elliott has recorded, skin cancer is much commoner in blonds than in brunets

DR PAUL E BICHET, Elizabeth, N J Dr Elliott and Dr Welton have made a valuable contribution to the therapy of cutaneous cancer I can heartily endorse their therapeutic measures, as my results with the same therapy during five years have been equally favorable (*Diagnosis and Treatment of Cutaneous Cancer, M Rec* **148** 50 [July 20] 1938) I have always been deeply impressed with the fact that solar radiation plays an important causative role in cutaneous cancer, and this opinion has been greatly influenced by the clinical and experimental corroborative data gleaned from the literature and presented by me before the Section of Dermatology and Syphilology of the American Medical Association in 1933 (*ARCH DERMAT & SYPH* **29** 221 [Feb] 1934)

No article on cutaneous cancer is complete without a bow to Dubreuilh, who first recognized in 1907 the possible etiologic role of excessive solar burns in the causation of epithelioma, or to that grand old clinician, Samuel Sherwell, of Brooklyn, who introduced acid mercuric nitrate after thorough curettage in the treatment of epithelioma (*J Cutan & Genito-Urin Dis* **5** 9, 1887)

DR DAVID A OLIVER, Chicago I personally am a good example of the person with the fair type skin in which epitheliomas develop For that reason, I have had a great deal of interest in skin cancer I agree entirely with Dr Elliott about the effect of solar radiation and climate

I wonder if you realize that even in Texas the cattle acquire carcinomas I visited the stockyards several years ago with Dr Klauder in search of cases of diamond back disease

In visiting the Bureau of Animal Industry, I was much surprised to see the skulls of a number of Texas longhorn cattle—also illustrations of them—with typical epitheliomas of probably a squamous cell type, at the inner canthus of the eye These carcinomas had extended into the skull and killed the animal

On questioning the curator in charge of the museum, he said it was very common for Texas longhorn cattle to have carcinomas

DR EVERETT S LAIN, Oklahoma City I have especially enjoyed Dr Elliott's and Dr Welton's presentation because I am personally one of those fair-complected persons who has to look out for skin cancers

The results of the United States Public Health cancer survey which has been made of Fort Worth and Dallas areas are doubtless much the same as might be shown for Oklahoma, plus, perhaps, a little more irritation from blowing sand, which furnishes an additional contributing factor It is generally accepted that chronic irritation from any cause is an important factor, and certainly excessive solar radiation is one of them

Therefore, the members of the Association are indebted to Drs Elliott and Welton for having brought such statistical evidence of possible effects of excessive sunlight on the skin, which is only a confirmation of a concept which has for a long time existed in minds of physicians who treat cancer I do not, however, think that sunlight has any appreciable effect on cancer in other organs of the body

The American Society for the Control of Cancer, which name was recently changed to The American Cancer Society, has been encouraging the United States Public Health Service to make such cancer surveys I am looking forward to the time when they will also make a cancer survey of Oklahoma Doubtless Oklahoma will show a parallel or similar frequency

The essayists also emphasize the heredity factor in skin cancer They reported that skin cancer is relatively infrequent in Negroes The same is also true in most of the pigmented races in all parts of the world

Some years ago, when I presented the subject of carcinoma of the lip before the Section on Dermatology and Syphilology of the American Medical Association, I called attention to the almost total absence of skin cancer in the American Indian though the Indian is exposed to all the severe elements of the weather I am speaking only of the full-blooded Indian The patient was a woman who had a cancer on the nose, who alleged, though I have reason to doubt it, that she was a full-blooded Indian

Also, it is interesting to note the relative infrequency of skin cancer in women, except farm women, doubtless because of protection offered by cosmetics

I was at first almost alarmed about the increased habit of smoking among women, though perhaps the lipstick is going to be their savior

Finally, all physicians recognize the successful method of treatment aims at the complete or total eradication of the neoplastic cell, whether it is surgical intervention, endothermy, electrocoagulation or radiation, and the success of the treatment largely depends on the particular perfected technic that the individual physician has developed If radiologists were present today they would tell of the greatly improved therapy—to which I can also testify—which has come about since the introduction of interstitial radium platinum needles Had Drs Elliot and Welton included cancer of the lip in their statistics, doubtless their percentage of cures would naturally be lower, Dr Elliott tells me that that subject is to be presented in a separate paper

DR EUGENE F TRAUB, New York One of the important things that Dr Elliott's paper brought out was the fact that he as a dermatologist followed and treated almost 2,000 patients with cancer over a period of five years and that his percentage of five year cures is an unusually high one

If I understood correctly, most of the lesions were treated by a combined method Recently at the New York Academy of Medicine a symposium on this subject was held, and two surgeons, two radiotherapeutists and two dermatologists were invited to discuss the subject The radiotherapeutists, of course, treated all

their lesions with radiation. One of them, in discussing the subject, stated that his doses of radiation to produce a cure were so great at times in order to effect this result in every type of epithelioma of the skin that if the lesion was originally basal cell one had to observe carefully that later a squamous cell lesion did not develop at the site because of the large dosage.

The surgeon explained that, even for the removal of small lesions, frequently extensive plastic repair was necessary, together with essential periods of hospitalization.

The dermatologist, in view of his training, is, in my opinion, best qualified to treat the majority of these lesions, and I am glad to hear that Dr Elliott was able to report better than 97 per cent cures over a five year period by a combination method that is certainly far superior to any one type of treatment employed by those familiar with only one remedy. The fact that dermatologists use a curet, of course, is sneered at and frowned on by both sides but, I am sure, simply because of ignorance of the use of one of the best adjuncts to the treatment of this disease.

The high percentage of squamous cell epitheliomas so successfully treated is another point that makes Dr Elliott's statistics more impressive. A high percentage of cures can always be obtained when one is dealing with basal cell lesions only, but since his report includes so large a number of squamous cell lesions it certainly adds to the excellence of his results.

DR ANTHONY C CIPOILARO, New York. It is late, and I dislike to prolong this discussion. However, the subject is an important one. I wish to congratulate Dr Elliott on his wonderful summary of a difficult subject. He has included everything that pertains to cancer of the skin.

Dr Traub discussed what I was going to discuss in relation to the methods of treating cutaneous malignant growths. I agree entirely with the method employed by Dr Elliott and with the remarks made by Dr Traub.

In relation to the causation of cancer, I should like to cite two authorities who have studied this subject very thoroughly.

Roffo, in Buenos Aires, has reported that about 95 per cent of all cutaneous malignant neoplasms occur on the face and the backs of the hands in other words areas of the skin exposed to the sun. He thoroughly believes that most cutaneous cancers are caused by exposure to rays of the sun, as brought out by Dr Elliott in his paper.

Paul and Molesworth, two brilliant Australian students of the subject, have stated that in a population made up of the same stock as in Great Britain, the incidence of cutaneous cancer is about ten times greater in Australia than it is in Great Britain. I did not make myself clear there. What I am trying to say is that the English people, transferred from the British Isles to Australia, show cancer ten times more frequently in Australia than they do in the British Isles. Both Molesworth and Paul tried to bring out the fact that ultraviolet rays are carcinogenic.

DR JAMES H MITCHELL, Chicago. Dr Elliott has given conclusive proof of the harmfulness of excessive exposure to the action of sunlight. While dermatologists are warning their patients of the danger of external applications, they should add sunlight to the list.

I have watched persons over the years exposing themselves to sunlight in excess on the golf course and about the swimming pool, and I have had them come in one after another with epithelioma.

DR JOSEPH A ELLIOTT, Charlotte, N C. I am indebted to the speakers for their discussion. Many of the things that have been brought out by the discussants

are included in our original paper, but time, of course, did not permit me to read them, as for instance, epithelioma in cattle Findlay found 170 cases of cancer in the skin of cattle, and all but 3 of the lesions occurred in white areas I think that this is significant

The cases that we reported were all of lesions of the skin and did not include lesions of mucous membranes Most of them were small lesions, as shown in our charts In the cure of small lesions it did not make any difference whether the lesion was of basal or of squamous cell type This, of course, is not true when the lesion is a large one

The choice of a method of treatment depends largely on the type, size and location of the cancer As was pointed out in our paper, we believe that lesions of the ear which involve cartilage should be removed surgically Most of our recurrent lesions were in this location, and some of them had to be referred to the surgeon for total excision

There are some advantages to living in a small city rather than in a metropolitan area One of these advantages is that one gets very much better cooperation from the men in one's profession This is due to the fact that one is personally acquainted with all of the physicians in the area Most of them refer their patients with epithelioma to the dermatologist for treatment On the other hand, if the dermatologist sees lesions that he thinks should be removed surgically, he refers them to a surgeon In that way one gets excellent cooperation

We do not treat all of our patients by any one method, but, briefly, the method we have employed most frequently is, first, thorough curettage of all the abnormal tissue followed by electrodesiccation or coagulation of the new surface Then the area thus treated, plus a peripheral margin of normal skin, is exposed to 600 to 800 r unfiltered roentgen rays This exposure is repeated at four to seven day intervals until a total of 3,000 r or more has been given We believe that this method of administering roentgen rays produces results superior to those when the same total dose is given at one sitting The time required for healing ranges from four to seven weeks depending on the original size and depth of the lesion

## POIKILODERMA ATROPHICANS VASCULARE JACOBI

Cutaneous Changes Typical of This Disease in a Patient with Late  
Meningovascular Neurosyphilis

FREDERICK KALZ, M D

AND

JAN HOOGSTATEN, M D

MONTREAL, CANADA

IN 1907 Jacobi<sup>1</sup> designated the symptom complex previously described by Petges and Clejat<sup>2</sup> as poikiloderma atrophicans vasculare. Many cases of this disease have since been described and in 1930 a complete critical survey of the literature was compiled by Oppenheim<sup>3</sup>. Several reports have been published on this continent, including papers by Taussig<sup>4</sup> and Oliver,<sup>5</sup> both reviewing the more recent literature.

The characteristic features of poikiloderma atrophicans vasculare are atrophy, telangiectasia and pigmentation. The atrophy causes a cigaret-paper-like thinning of the skin, and the telangiectasia and pigmentation form a colorful pattern, resembling at times atrophy of the skin due to roentgen rays. This condition has been observed in combination with myositis and scleroderma.

There has been considerable controversy as to whether poikiloderma atrophicans vasculare is a separate entity or whether it is an early or end stage of other diseases of the skin. Mycosis fungoides and lymphosarcoma have produced similar even clinically indistinguishable pictures, making diagnosis difficult. In addition, nevroid disorders and cutaneous atrophies due to photosensitization may present similar pictures.

The types described are designated as follows:

1 Poikiloderma atrophicans vasculare (Jacobi<sup>1</sup>)

2 Poikilodermatomyositis (Petges and Clejat<sup>2</sup>)

From the Section of Dermatology, Department of Medicine J. C. Meakins, M.D., Physician-in-Chief, and the Department of Pathology, T. R. Waugh, M.D., Pathologist-in-Chief, Royal Victoria Hospital, Montreal, Canada.

1 Jacobi, E. Poikiloderma atrophicans vasculare, *Ikonog Dermat* **3** 95, 1908.

2 Petges, G., and Clejat, H. Sclerose atrophie de la peau et myosite generalise, *Ann de dermat et syph* **7** 550, 1906.

3 Oppenheim, M., in Jadassohn, J. *Handbuch der Haut- und Geschlechtskrankheiten* Berlin, Julius Springer, 1931, vol 8, pt 2, pp 635-649.

4 Taussig, L. Poikiloderma atrophicans Vasculare Jacobi. *Arch Dermat & Syph* **25** 882 (May) 1932.

5 Oliver, E. A. Mycosis Fungoides with Poikiloderma-Like Symptoms, *Arch Dermat & Syph* **33** 267 (Feb) 1936.

- 3 Scleropoikiloderma (Rottmann,<sup>6</sup> Jaffe<sup>7</sup>)
- 4 Congenital poikiloderma, a nevoid disorder of the skin (Thomson<sup>8</sup>) previously described by Zinsser, Janovsky, Jadassohn, Lutz and others and reviewed in Oppenheim's survey<sup>3</sup>
- 5 Poikiloderma of Civatte,<sup>9</sup> identical with pigment melanosis (Riehl<sup>10</sup>)
- 6 Cutaneous changes morphologically resembling those of poikiloderma atrophicans vasculare, eventually leading to lymphosarcoma (Lane<sup>11</sup>) or to fungoides (Oliver<sup>5</sup>)
- 7 Poikiloderma-like end stages of various eruptions healing with atrophy—(Muller<sup>12</sup>), poikiloderma erythematodes reticulare

End stages of cutaneous syphilis may show atrophy and pigmentary changes. Telangiectasia has not been described in such cases. Van der Valk<sup>13</sup> described such cases under the heading of "leucotrophia syphilitica Fournier." Hudelo and Cailliau<sup>14</sup> and Thibierge and Hufnagle<sup>15</sup> presented cases of this disease in syphilitic persons who displayed erythematous and atrophic plaques, in both instances the cutaneous changes belong in the group of dermatitis atrophicans maculosa.

The first three variations are considered as a clinical entity.

Recently we had the opportunity of investigating a patient who presented a clinical picture similar to those described by Jacoby.<sup>1</sup>

#### REPORT OF A CASE

A 45 year old Canadian, of Scottish extraction, had a positive Wassermann reaction in the blood donor clinic at the Royal Victoria Hospital. He was unaware of his syphilitic infection. He stated that twelve years previously he had suffered

6 Rottmann, H. G. Ueber Poikilodermie mit bemerkenswerten Nebenbefunden, *Arch f Dermat u Syph* **153** 747, 1927

7 Jaffe, K. Falle von Sklero-Poikilodermie, *Arch f Dermat u Syph* **159** 257, 1930

8 Thomson, S. Poikiloderma Congenitale, *Brit J Dermat* **48** 221, 1936

9 Civatte, A. Poikilodermie reticulée pigmentaire, *Ann de dermat et syph* **6** 705, 1925

10 Riehl, C. Pigment Melanosis, *Wien klin Wchnschr* **30** 780, 1917

11 Lane, J. E. Poikiloderma Atrophicans Vasculare, with Report of a Case by Oliver S. Ormsby, M.D., Chicago, *Arch Dermat & Syph* **4** 563 (Nov) 1921, Poikiloderma Atrophicans Vasculare. Conclusion of Previously Reported Case, *ibid* **8** 373 (Sept) 1923

12 Muller, H. Lupus Erythematosus mit Atrophien, *Zentralbl f Haut- u Geschlechtskr* **3** 130, 1922

13 Van der Valk, W. Leucotrophia syphilitica Fournier, uber Leukodermie, *Zentralbl f Haut- u Geschlechtskr* **17** 416, 1925

14 Hudelo, H., and Cailliau, A. Examen histologique d'un cas d'atrophie maculeuse, *Bull Soc franç de dermat et syph* **28** 372, 1921

15 Thibierge, G., and Hufnagle, H. Erytheme en plaques atrophiant et sclerodermisant, *Bull Soc franç de dermat et syph* **28** 328, 1921



from violent headaches, that his left eyelid drooped and that his vision was impaired. In 1935, bluish spots appeared on the skin of the arms, the legs and the trunk, and a gradual darkening of the areas involved was noted. There was no pruritus or subjective sensation other than coldness of the left hand.

Examination revealed a slight ptosis of the left eyelid, slight pallor of the left disk and reduced vision of the left eye. Visual fields and pupillary reactions were normal. Knee and ankle jerks were not elicited, and vibratory sense was reduced.

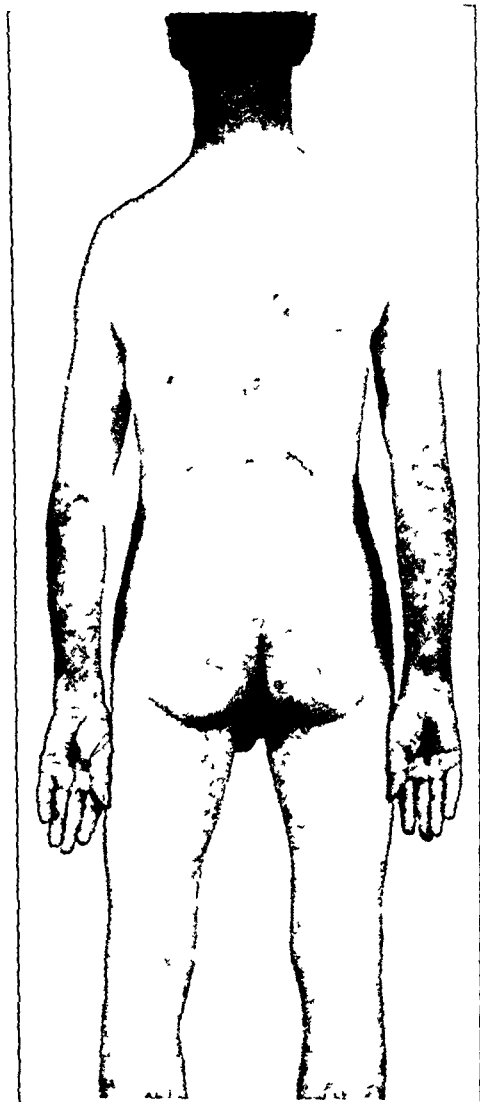


Fig. 1—Back, buttocks and forearms showing large areas of pigmentation with sharply demarcated borders and discrete patches of normal skin.

in the left leg. No further abnormalities were found, with the exception of the cutaneous changes, which will be described in detail later.

The Wassermann reaction of the blood was positive in a serum dilution of 1:256. Examination of the spinal fluid revealed that the first zone was positive with 0.1 cc. The colloidal gold curve was of the dementia paralytica type, being 555321000. There was no increase in cells, the result of the Pandy test was negative, and total proteins were 55 mg per hundred cubic centimeters.

A diagnosis of late meningovascular neurosyphilis was made.

The skin presented the following picture. Large areas of light brown pigmentation covered the shoulder blades, extending to the arms and involving most of the back and buttocks (fig 1). Equally large areas were noted on the chest and abdomen, these pigmentations were sharply demarcated, with a few discrete spots of normal skin. Part of the back showed superficial atrophy (cigaret-paper-like thinning of the skin) as well as lichenification and fine desquamation. The



Fig 2—Extensor surface of left arm, showing atrophy and telangiectasia

skin of the chest appeared normal, except for the pigmentation and some small angiomas of senile type, occurring both in normal and in pigmented skin.

Both forearms displayed changes of a different type. In addition to sharply outlined and partially atrophic areas, telangiectases and extravasation of blood were present, resulting in a curious mottled appearance which resembled roentgen atrophy. These changes were especially evident on the elbows (fig 2) and around an old vaccination mark on the left arm.

The skin of the left hand and wrist revealed a decided diffuse cyanosis, edema and slight atrophy but no pigmentation or telangiectasia. These changes corresponded clinically to acrodermatitis atrophicans chronica (Herxheimer)—a feature occasionally observed in poikiloderma atrophicans vasculare.<sup>3</sup>

There were numerous small pigmented areas with peripheral desquamation on the thighs, especially near the inguinal folds, and telangiectasia and atrophy, similar to those on the elbows, were observed on the extensor surfaces of the thighs, the ankles and the right knee.

Histologic examination of skin and subcutaneous tissue from the lesions on the back showed the epidermis to be thrown into broad irregular folds over the underlying dermis. For the most part, the epithelium was atrophic, with loss of rete pegs in some places. The horny layer was not appreciably thickened and was arranged in rather loose layers. The granular cells were still to be seen but were in a single flattened row. Beneath, the prickle cells were only two to six layers deep, and many were swollen and edematous. The usual sharp distinction between epidermis and corium was lost in many places and scattered leukocytes infiltrated the epithelial layer. The papillary bodies and subpapillary layer of the corium contained many mononuclear cells almost entirely lymphocytic, with practically no plasmacytic forms. A moderate degree of edema was present. A few widely dilated vascular channels were seen in the upper portion of the corium, and here special stains for elastic tissue showed that it had disappeared while the lower portion of the corium showed no special histologic changes. Occasional histiocytes containing granules of brownish pigment were found in areas of hyperemia, but no hyperpigmentation of the epidermis had occurred.

Sections of brownish firm tissue from the latissimus dorsi muscle did not show any pathologic changes.

Sections of skin and subcutaneous tissue from the elbow showed the horny layer to be slightly thickened and arranged in lamellar fashion, with a minimal amount of parakeratosis. The underlying granular layer was present and normal, while the prickle cell layer was thinned. In some places the cells of the basal layer were edematous and had swollen nuclei. The rete pegs were atrophic and in many places completely lacking, and the usual sharp distinction between epidermis and corium was absent. The upper part of the corium was edematous and infiltrated with mononuclear cells. A striking feature was the presence of many thin-walled dilated blood vessels just beneath the epidermis (fig. 3).

It should be noted that the mononuclear cell infiltration both in the section from the back and in the section from the elbow was arranged in the fashion of a reticular network, particularly about the blood vessels. Few, if any, plasma cells were seen. Some pigmented histiocytes were encountered. Again, special stains for collagen and elastic fibers revealed a decided decrease of the latter in the upper part of the corium, and in this region the collagen is poorly stained and appears swollen and hyaline in some areas.

The histologic picture was similar to that which has been described in poikiloderma atrophicans vasculare (Jacobi).

The myositis which is often observed in cases of this disease was lacking in the muscle tissue examined in this case.

Determinations of blood nonprotein nitrogen, creatinine, cholesterol and uric acid and the protein balance and sugar tolerance tests were within normal limits. A hemogram showed lymphocytosis and monocytosis, a reduced neutrophil count, a moderate anemia and an increased sedimentation rate findings compatible with those of neurosyphilis.

Roentgen examination of the chest and the skull did not show any pathologic changes

Antisymphilitic treatment was started with weekly injections of bismuth subsalicylate in oil (2 cc [0.2 Gm of the drug]) followed by weekly injections of oxophenarsine hydrochloride (0.06 Gm). During this time, eight weeks, a decided fading of pigmented areas was observed. Ten sessions in the fever cabinet, combined with injections of bismuth subsalicylate and oxophenarsine hydrochloride were subsequently given (fifty hours over 105 F). During this period all cutaneous lesions gradually disappeared, and at the conclusion of the fever therapy the skin

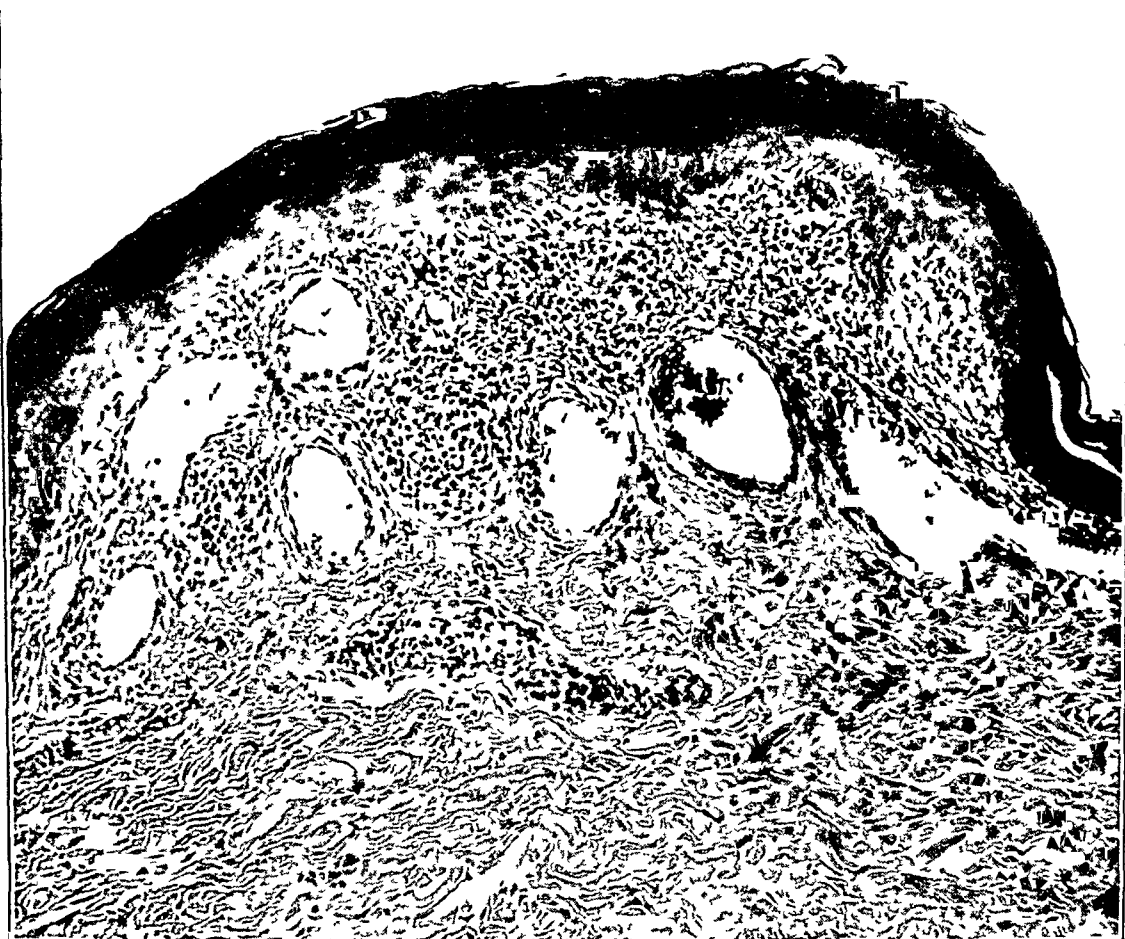


Fig 3—Section of skin and subcutaneous tissue from elbow, showing epithelial atrophy, round cell infiltration and many thin walled dilated blood vessels

appeared to be normal. The only residual lesions found were slight telangiectasia on the right elbow. There was no pigmentation or atrophy, and especially noteworthy was the reversal of the circulatory changes of the right hand, which prior to treatment was edematous, blue and cold.

This effect of antisymphilitic therapy and hyperpyrexia was unexpected and puzzling. Histologic examination corroborated the clinical observations.

A section of skin and subcutaneous tissue taken from the elbow several months after therapy was instituted showed that the epidermis was thrown into

irregular undulations. All layers were well defined but somewhat atrophic. The rete cones were generally absent, giving a flattened basal layer. The corium beneath showed no edema or exudate but contained long streaks of cells which were found to be remains of collapsed vascular channels and spaces (fig 4). Compressed flattened perithelial elements surrounded them. No pigment was seen, and no sudoriferous or sebaceous glands were present. Stains for elastic tissue showed fibers in all but the closest subepidermal area.

Sections of skin and subcutaneous tissue from the back showed much the same picture, except that the streaks of endothelial cells lining collapsed vascular



Fig 4—Section of skin and subcutaneous tissue taken from elbow after institution of antisiphilitic therapy and completion of fever treatments, showing disappearance of round cell infiltration and collapse of vascular channels.

channels were lacking. Small open capillaries were present as well as some atrophic-appearing hair follicles and sudoriferous glands. No pigment was seen.

Comparison with sections removed before institution of antisiphilitic therapy shows the following striking differences: (1) loss of all edema, (2) collapse of vascular channels, (3) return of sharp definition between epidermis and corium, (4) disappearance of pigment and (5) increase in elastic tissue.

## COMMENT

Poikiloderma atrophicans vasculare is thought to be a therapy resistant disease. Oppenheim stated that *restitutio ad integrum* has not been reported, later in 1931, favorable results were observed by Fuhs and Konrad<sup>16</sup> with Grenz ray therapy and the following year Geiger and Konrad<sup>17</sup> reported a case in which this form of treatment resulted in the return of atrophic areas to normal and confirmed this point by histologic examination.

In our case, the following explanations for the unexpected and complete cure of this long-standing and widespread disease may be considered.

1. Clinical cure in a characteristic case of Jacobi's disease was brought about by the nonspecific effect of arsenical drugs and hyperpyrexia. Arsenic in the form of solution of potassium arsenite U. S. P. has been known to exert some beneficial effect on this eruption but we could not find in the literature a report of cure in a case of advanced disease. Hyperpyrexia, to our knowledge, has never been used in treating this disease.

2. The cutaneous changes observed in this case represent a hitherto undescribed disorder of the trophic-vascular type, caused by a meningo-vascular neurosyphilis and cured by the specific action of the antisiphilic therapy on the central lesion.

There may be found in the literature some evidence supporting the possibility that a lesion of the central nervous system is a causative factor. Pardo-Castello<sup>18</sup> described a case of Jacobi's disease in a man with neurosyphilis, but the result of treatment was not given. Masslow<sup>19</sup> reported a case in which trophic cutaneous changes and telangiectasia occurred after trauma to the thalamic region.

Involvement of the pituitary gland has occasionally been observed in these cases, and several instances are cited in Taussig's paper<sup>4</sup> and reported by Montgomery and O'Leary<sup>20</sup>. Anatomic changes could not be demonstrated in our case by roentgenologic examination of the skull, but the long-standing neurosyphilis may well account for a parenchymatous lesion.

16 Fuhs, H., and Konrad, J. Grenzstrahl-Hauttherapie, Berlin, Urban & Schwarzenberg, 1931.

17 Geiger, R., and Konrad, J. Ist die Poikilodermie atrophicans vasculare ein selbstaendiges Krankheitsbild, Dermat. Wchnschr. **94** 34, 1932.

18 Pardo-Castello and Lopez, C. Poikiloderma Vascular Atrophicans, Bol. Soc. de dermat. y sif. **2** 207, 1941.

19 Masslow, P. Ueber einen Fall von Erythromelie Pick nach Verletzung des Thalamus opticus, Arch. f. Dermat. u. Syph. **170** 303, 1934.

20 Montgomery, H., and O'Leary, P. A. Poikiloderma Atrophicans Vasculare Arch. Dermat. & Syph. **25** 942 (May) 1932.

## SUMMARY

A case of clinically typical poikiloderma atrophicum vasculare in a patient with meningovascular neurosyphilis has been described.

The histologic changes were characteristic of this disease, the main features being epithelial atrophy, edema, pigmentation, abundance of thin-walled blood channels and a peculiar dense reticular perivascular mononuclear infiltration.

Arsenical therapy with hyperpyrexia was followed by almost complete disappearance of all cutaneous lesions, including telangiectasia and atrophy.

The disappearance of the cutaneous lesions may be explained by the nonspecific effect of the arsenical drug combined with hyperpyrexia or by the fact that the patient had a hitherto undescribed trophic vascular disease of central origin, clinically and morphologically indistinguishable from the disease described by Jacobi, which responded to antisyphilitic therapy.

T. R. Waugh, M.D., and Mr. Brian Thomlinson, department of pathology, cooperated in this study.

## EXPERIMENTAL STUDY ON THE ABSORPTION OF AMYLOID IN LOCALIZED AMYLOIDOSIS BY SKIN GRAFTING

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NUMEROUS experiments have been made on animals in order to clarify the question of the origin and absorption of amyloid. The results of these experiments seem to indicate that experimentally produced deposits of amyloid can be made to disappear.

A few observations have been made on human beings, but only in the case of generalized amyloidosis has evidence been encountered for the definite disappearance of amyloid from certain sites.

Waldenstrom,<sup>1</sup> in several biopsies of spleens and livers of 10 patients with generalized amyloidosis noted in all of them the gradual, occasionally complete disappearance of deposits of amyloid. In another article, he added the results of histologic studies, revealing the disappearance of amyloid which had been present before. Metraux,<sup>2</sup> in an autopsy of a patient in whom amyloidosis had been temporarily cured clinically, recorded changes in the liver and spleen indicative of the absorption of amyloid. There were patches of granulation tissue with finely distributed amyloid and further phagocytosis in Kupffer's stellate cells.

Another method to determine the partial or complete disappearance of amyloid is Bennholt's intravenous congo red test. Harmon and Kernwein<sup>3</sup> showed in 2 cases and Haben<sup>4</sup>, Rosenblatt<sup>5</sup> and Reimann<sup>6</sup>

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1 Waldenstrom, H. Ueber das Entstehen und Verschwinden des Amyloids beim Menschen. *Klin. Wchnschr.* **6**: 2235-2237 (Nov. 19) 1927, Formation and Disappearance of Amyloid in Man, *Acta chir. Scandinav.* **63**: 479-530, 1928.

2 Metraux, P. Ueber Rückbildungsvorgänge bei menschlicher Amyloidose, *Frankfurt Ztschr. f. Path.* **37**: 279-292, 1929, cited by Koenigstein.<sup>8</sup>

3 Harmon, P. H., and Kernwein, G. Utility of Congo Red Test in Diagnosis and in Differential Diagnosis, *Arch. Int. Med.* **70**: 421-433 (Sept.) 1942.

4 Haben, H. C. Amyloidosis. Report of Case in Which Patient Recovered, *Proc. Staff Meet., Mayo Clin.* **9**: 261-262 (May 2) 1934.

5 Rosenblatt, M. B. Recovery from Generalized Amyloidosis Secondary to Pulmonary Tuberculosis, *Arch. Int. Med.* **57**: 562-565 (March) 1936.

6 Reimann, H. A. Recovery from Amyloidosis, *J. A. M. A.* **104**: 1070-1071 (March 30) 1935.



in 1 case respectively this reversal of the color test. Harmon and Keinwein report a total of 11 cases in which actual cures were effected, including the 5 cases aforementioned, another 4 of Waldenstrom and 2 of Pearlman.<sup>7</sup> Koenigstein,<sup>8</sup> discussing the absorption of amyloid, pointed out that the experimental as well as the clinical experience so far available is not conclusive. Although evidence was found that reabsorption may start and minor deposits may disappear, regular dissolution of extensive accumulations has not been proved.

In the literature dealing with the question of the absorption of amyloid from the skin, Freudenthal<sup>9</sup> has reported on the histologic changes in lichen amyloidosis and senile amyloidosis. He found amyloid deposited intraepidermally and in the horny layer and in addition a row of amyloid deposits extending vertically from the basal layer through the epidermis to the horny layer; he suggested this as evidence that small fragments of amyloid which have by some means penetrated into the basal layer are lifted together with the other cells and are eliminated through the horny layer.

The following is a brief description of an experimental study of the behavior of amyloid in pedunculated and free skin grafts.

The procedure was to transplant a skin flap which showed a positive staining reaction to an intracutaneous injection of congo red to an area with a negative reaction and vice versa. The experiment was made on a patient who voluntarily placed himself at my disposal for this purpose.

#### REPORT OF A CASE

The patient was a man of 66 examination of whom revealed no indication of any general disease but who was suffering from amyloidosis of the legs which he had had for thirty years. (As to the details see case 1 in the report by Dostrovsky and Sagher<sup>10</sup>) For three years he had been under clinical observation. He was admitted to the hospital on March 17, 1941. On the anterior and lateral surfaces of the legs, extending from the region of the knees down to the ankles, there were nodules of a reddish yellow to grayish brown color. On the posterior surfaces only the distal thirds were involved, while the region of the triceps surae (calf) muscle was normal. The reaction to an intracutaneous injection of congo red was positive in the distal portions of the legs (fig 1 A), while in the proximal

7 Pearlman, A. W. Regression of Amyloidosis, *Quart Bull Sea View Hosp* 6: 92-97 (Oct.) 1940.

8 Koenigstein, H., in Jadassohn, J. *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1932, vol. 4, p. 3.

9 Freudenthal, W. Amyloidbefunde in der Haut, *Zentralbl f Haut- u Geschlechtskr* 20: 26, 1926, Verruca senilis und Keratoma senile, *Arch f Dermat u Syph* 152: 505-528, 1926, Rumpfhautepitheliom (nebst Bemerkungen über die Verruca senilis und das Keratoma senile), *ibid* 158: 538-544, 1929, Amyloid in der Haut, *ibid* 162: 40-94, 1930.

10 Dostrovsky, A., and Sagher, F. Localized Amyloidosis of Skin. Report of Cases, Intracutaneous Congo Red Test as Diagnostic Aid, *Arch Dermat & Syph* 44: 891-906 (Nov.) 1941.

portions it was definitely negative. The areas involved were thoroughly tested in order to establish their precise borders (fig 1 B).

On March 26, 1941, the following operation was performed by Professor Mandl. On the posterior surface of the right leg the skin, including the entire cutis and subcutis, was shifted in Z fashion, the diagonal incision being approximately 15 cm long and the two horizontal ones approximately 6 cm each. The operation was carried out with the area under local procaine hydrochloride anesthesia. Figure 1 B contains a schematic representation of the manner in which the skin flaps were shifted. At the same time a small piece of skin was transplanted as a free graft to a remote site (loin region) but did not take. During the operation, tissue was taken for histologic examination from both skin flaps.

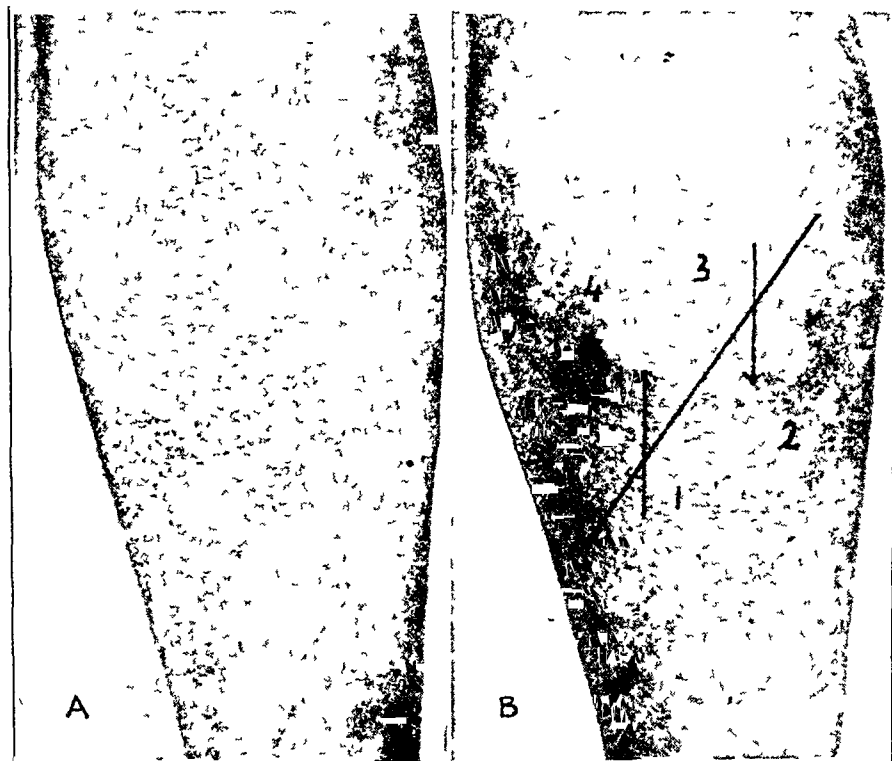


Fig 1—A, posterior surface of the right leg showing, in its distal portion, a positive reaction to Congo red. B, delimitation of the amyloid-containing areas by the Congo red test. Note the four points at which the dyestuff was injected, which, however, was retained by the nodules in the distal portion only. The sketch shows the manner in which the skin flaps were shifted.

*Histologic Examination* (Institute of Pathology, Head, Professor Franco) — (A) Specimen of Skin Yielding a Positive Intracutaneous Congo Red Reaction. There was distinct atrophy of the epidermis, and the rete Malpighii was thinned out, with an absence of cones at several places, those present showing irregular hypertrophy. Universal hyperkeratosis was noticed.

Underneath the epithelial layer there were numerous areas containing disorderly distributed accumulations of a substance staining yellow-orange with Van Gieson's stain and pale pink with Bismarck brown (amyloid), side by side with cells which showed the results of pressure, among them numerous chromatophores. The blood vessels were dilated and congested, some of them surrounded by a slight

degree of cell infiltration. The sweat glands appeared normal. No hairs or sebaceous glands were present.

(B) Specimen of Skin Yielding a Negative Intracutaneous Congo Red Reaction. The changes were the same as those previously indicated, i. e., the specimen also contains amyloid-positive islets. There were, however, a few hairs and sebaceous glands. The absence of elastic fibers was noted at two places where amyloid was present.

Amyloid was, therefore, present not only in the regions with positive reactions to congo red but in those with negative ones too.

*Development*—Healing was slightly delayed by the tension to which the flaps were exposed. As a rule, grafts are made one third larger than the area they



Fig 2—The upper flap is now below and vice versa. Note considerable scarring at tips of flaps. At the points marked 1 and 2, amyloid nodules are still recognizable three and a half years after transplanation. At the points marked 3 and 4 no new formation of amyloid has taken place. Note the multitude of nodules with positive reaction to congo red distally to 3 outside the site of operation.

are intended to cover so that no tension may be exerted on the sutures, but in my case this was technically impossible. Owing to this tension, rather extensive scarring occurred at the tips of both flaps. In the photographs this makes it difficult to recognize the positive results (fig 2).

The patient was discharged on May 23, 1941 and remained under constant supervision. Every two to three months, tests were made (at the places marked 1, 2, 3 and 4), the last one being made on Aug 1, 1944.

The question I intended to clarify was whether in the course of time the flap of skin originally with a negative reaction to congo red would adapt itself to its new positive environment.

In order to insure the greatest possible degree of accuracy, the tests were made in precisely the same four areas every time. In the figure 1 indicates the medial part of the distal flap which was decidedly positive (fig 1A). It had been shifted proximally into a negative area. The reaction to congo red remained positive. The lateral portion of the distal flap, the reaction of which also remained positive to the congo red, is indicated by 2, the lateral portion of the proximal flap, originally negative and remaining negative, is indicated by 3, and 4 indicates the medial portion of the proximal flap, originally negative and also remaining negative.

These were the results obtained invariably throughout the entire period of observation, extending over three and a half years. It should further be pointed out that neither distally nor proximally to the site of operation did penetration or absorption of amyloid occur.

In the scars, the congo red reaction disappeared, a phenomenon already referred to in an earlier publication (case 4)<sup>10</sup>

#### COMMENT

In a case of localized amyloidosis (lichen amyloidosis) skin grafts were made in order to study, by the help of the intracutaneous reaction to congo red, the behavior of deposits of amyloid in a new environment. In the course of three and a half years, the areas with positive reactions to congo red, although now surrounded on all sides by tissue with a definitely negative reaction remained positive and the originally negative areas remained negative, although their entire neighborhood was sown with small nodules with positive reactions to congo red. Changes were noted only in places where the skin flaps became subject to necrosis and subsequent scarring owing to the considerable tension exerted on them after operation, in these scars the reaction became negative.

The fact that histologically in the areas with negative reactions to congo red as well as in the areas with positive reactions a positive amyloid reaction with Bismarck brown-gentian violet could be elicited seems somewhat disturbing. We had already encountered similar conditions on an earlier occasion but have been unable to find any reference to such a discrepancy in the literature. In case 2 of an earlier publication<sup>10</sup> the patient had on her back and extremities dark, grayish brown spots yielding a negative reaction to congo red while histologically amyloid could be identified in them. The reverse occurred in case 3, in which within a poikilodermal area on the leg a positive reaction to congo red could be elicited while histologically no amyloid could be demonstrated.

Discrepancies of the microchemical, histologic reactions have also been referred to by Gans<sup>11</sup> who noted that amyloid may occasionally show only metachromasia while another type yields a positive reaction.

<sup>11</sup> Gans, O. *Histologie der Hautkrankheiten*, Berlin, Julius Springer, 1925, vol 1.

to the iodine-sulfuric acid test only. Schmidt<sup>12</sup> expressed the opinion that it is the age of the deposit that should be interpreted in such a way that fresh amyloid might yield the former and older deposits the latter reaction.

The intravenous congo red test is quantitative, but small quantities cannot be detected by this method. The intracutaneous method is both qualitative and quantitative, facilitating the detection of insignificant deposits of amyloid in the skin, which in the intravenous method would not have influenced the absorption time from the blood.

If therefore, skin tests elicit negative reactions although amyloid is demonstrated histologically, the reason must be looked for in certain chemical or morphologic properties of the type of amyloid present. It might be imagined that the particles of amyloid in these areas are so small that their positive reaction is not recognizable either by the naked eye or through the magnifying glass or that its chemical structure is of such a nature as to yield a positive reaction in the microscopic section only.

The first assumption can be disproved by the fact that even the deposits consisting of minute particles of amyloid would be expected to produce a certain degree of discoloration on the introduction of congo red, which should, moreover, remain there for some time, as is usually the case with the positive reaction to congo red. But this is not so. The color disappears rapidly (within forty-eight hours) in the same way as in other cases with negative reactions, while in regular amyloid nodules it continues to be present for a fortnight or even longer.

Amyloid belongs to a group of protein bodies the chemical structure of which is not yet understood. Similarly, because it is still undecided whether strictly local amyloidosis and the generalized variety are one and the same process, the constitution of amyloid in the various organs is still the object of discussion.

Possibly one is witnessing the different phases of protein metamorphosis (Gans), a theory deduced from the discrepancies in the chemical behavior of microscopic amyloid. This theory receives support from differences I have outlined between vital and microscopic stains.

From my experiment it therefore appears that amyloid-containing skin yielding a positive reaction to an intracutaneous injection of congo red does not lose this reaction after having been transplanted to another site and vice versa. The experiment also throws some light on the pathogenesis of amyloidosis. The typical site of localized amyloidosis is on certain areas of the legs, the skin here apparently possessing qualities likely to favor amyloidosis. It could be shown that a skin flap containing this type of amyloid and transplanted to another area

<sup>12</sup> Schmidt, cited by Gans<sup>11</sup>

of the skin retained its amyloid. This fact suggests that local conditions are the decisive factor in the production of localized amyloidosis, since in the generalized variety absorption seems to be proved.

#### SUMMARY

In a patient with localized amyloidosis of the skin, the absorption of amyloid or its possible appearance in other sites was studied by the surgical transplantation of pedunculated skin flaps.

Flaps which had originally shown a positive reaction to congo red were shifted to an area with a negative reaction and vice versa. In the course of three and a half years, the reaction remained unchanged even in the transplanted skin flaps. No new formation or absorption of amyloid was noted. The essential factor in the pathogenesis of the disease is apparently a local one in a particular site.

A free transplantation of pieces of skin was unsuccessful.

Attention is drawn to discrepancies appearing in the vital stains with congo red and the histologic stains with Bismarck brown—gentian violet, the reason for which seems to lie in the chemical structure of the particular amyloid present.

Professor Mandl, Head of Surgical Department B, and Professor Franco, Director of the Institute of Pathology, cooperated in the experiment.

# UNUSUAL PIGMENTATION DEVELOPING AFTER PROLONGED SUPPRESSIVE THERAPY WITH QUINACRINE HYDROCHLORIDE

LIEUTENANT COLONEL CHARLES H LUTTERLOH

AND

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ANY physician who has had experience with the administration of quinacrine hydrochloride (atabine) for malaria is familiar with the lemon yellow pigmentation of the skin which at times accompanies the use of this drug. It is also known that this pigmentation is due to the staining of the tissues by quinacrine, a dye, and disappears within a reasonable time after the drug is discontinued. This well known observation furnished the clue to the unusual pigmentation which was noted at uncommon sites in a group of patients.

Our interest in the present problem was brought about when one of us (C H L) in March 1945 had the opportunity of observing a patient who presented a peculiar discoloration of the nails of the hands and feet. This patient stimulated our interest and caused us to be on the alert for a similar discoloration in other patients. From March through July 1945, we had the opportunity of making similar observations on 7 other patients. All of them had seen long service in the Southwest Pacific areas and had taken quinacrine hydrochloride consistently as a suppressive measure for a number of months. Six of the 8 patients came from the same division and the other 2 from a neighboring division, whose environmental conditions were the same and quinacrine suppressive medication similar. Three of these cases will be reported in detail.

## REPORT OF CASES

CASE 1—A captain in the Field Artillery, aged 32, with four years and five months of service, thirty-three months of which were spent in the Southwest Pacific Area was admitted to the hospital on March 3, 1945 because of a dental problem, inanition, weakness and loss of weight. On physical examination, we were particularly impressed with the blue-gray, slate-colored pigmentation of the nails of the fingers and toes. The pigmentation seemed to be located not in

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the nail plate but in the nail bed. It occurred in one of two ways: either as a diffuse pigmentation involving the entire nail bed, this being the more frequent, or as a transverse band near the middle of the nail (figs 1 and 2). The officer also showed a rather pronounced lemon yellow pigmentation of the skin, of similar hue to that seen in patients receiving quinacrine therapy.

This officer had taken quinine sulfate, 10 grains (0.65 Gm.) daily, as a suppressive antimalarial measure for one month about July 1943. Then no suppressive therapy was carried out until September, at which time quinacrine hydrochloride tablets, 0.1 Gm. each, were administered in a dosage of 10 to 14 tablets per week and continued in this dosage until March 1945, or until time of admission to the hospital. The patient first noted the discoloration of the nails in September 1944, one year after the start of the suppressive therapy, and his first impression was that he had mashed his fingers. After five weeks' hospitalization there was no clearing of the pigmentation of the nails, however, there was a rather decided clearing of the skin. With the correction of the dental problem, rest and measures for his general health he was much improved and shortly thereafter was returned to duty.

This officer during his overseas service had two attacks of chills and fever. Smears of blood revealed no plasmodia during both illnesses, and one of the two attacks was thought to be dengue.

Tests made gave the following results. The Rumpel-Leede phenomenon was negative. The fragility of the red blood cells and the platelet count were normal. The Wassermann and Kahn reactions were negative and repeated smears revealed no evidence of malaria. The results of cephalin flocculation and hippuric acid tests, total proteins, albumin-globulin ratio, icterus index, prothrombin time, cholesterol and cholesterol esters were found to be within a normal range. Urinalyses and studies of urea nitrogen and urea clearance revealed no abnormalities. A voided specimen of urine was kept for twenty-four hours, and there was no change of color noted from brown to black, which would indicate the presence of homogentisic acid.<sup>1</sup> Ochronosis accompanying alkaptonuria was further ruled out by the Fishberg test.<sup>2</sup> Studies of the urine for melanin pigments were not made, possibly they would have given constructive information. Determinations of vitamin C in the plasma were within a normal range. A biopsy was considered, but permission for it could not be obtained.

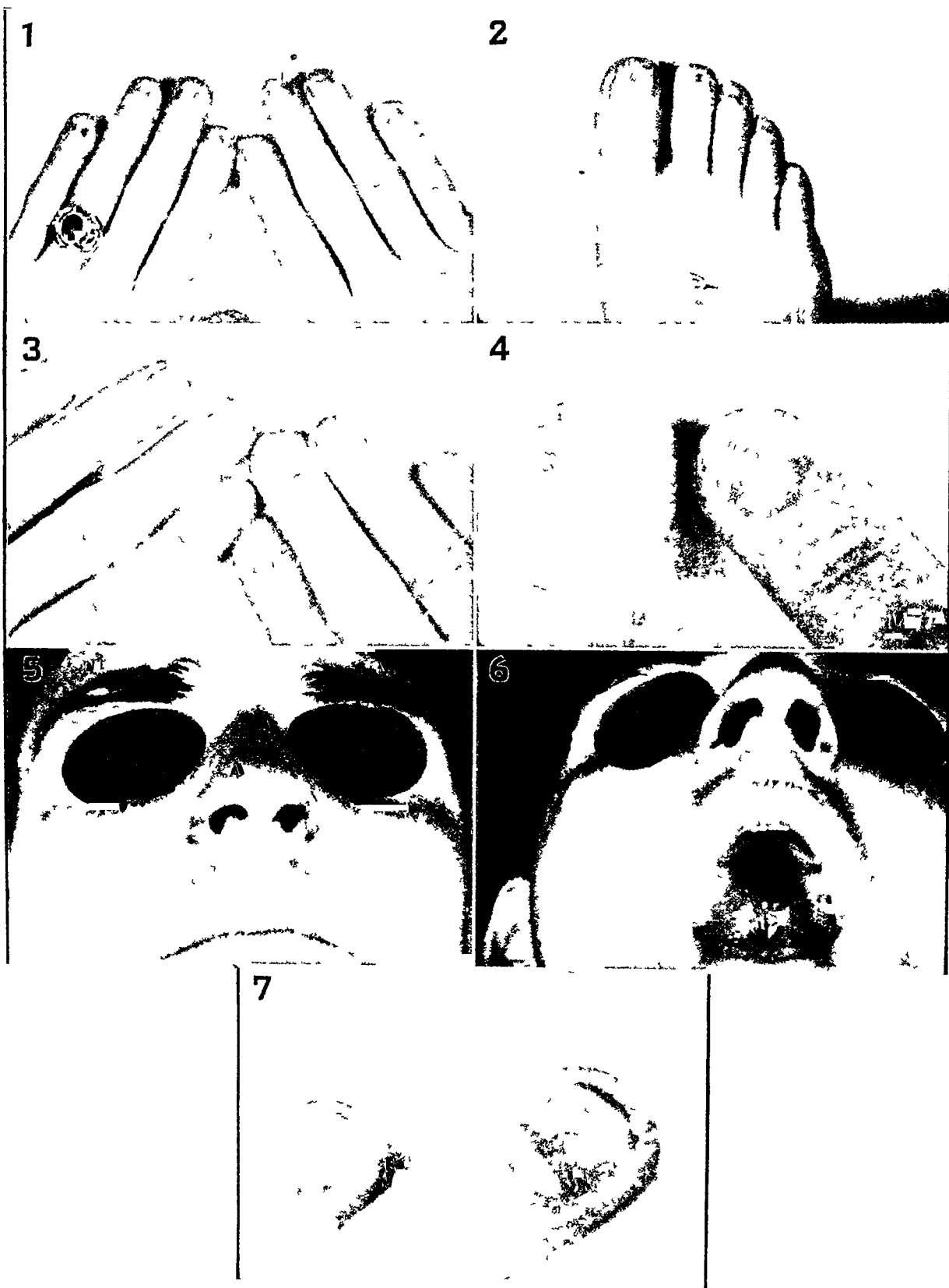
This patient was again seen in July 1945, about four months after his admission to the hospital, during which period he had taken no quinacrine hydrochloride. We were greatly encouraged because at this time the abnormal pigmentation had cleared considerably, the transverse bands being not so prominent and the diffuse pigmentation giving the nail a much lighter color. The transverse bands, however, occupied the same relative position, thus confirming our original impression that the pigment was not in the nail itself. Clinically, the improvement was definite, and even in the Kodachromes (figs 3 and 4) the change is rather striking.

CASE 2—A corporal in the Field Artillery, same division as the first patient, aged 29, with four years and nine months of service, thirty-seven months in the Southwest Pacific Area, was referred to us as an outpatient from the Separation

1 (a) Smith, J. W. Ochronosis of Sclera and Cornea Complicating Alkaptonuria. Review of the Literature and Report of Four Cases, *J. A. M. A.* **120** 1282-1288 (Dec. 19) 1942. (b) Jeghers, H. Pigmentation of the Skin, *New England J. Med.* **231** 88-100, 122-136 and 181-189, 1944.

2 Fishberg, E. H. The Instantaneous Diagnosis of Alkaptonuria on a Single Drop of Urine, *J. A. M. A.* **119** 882 (July 11) 1942.





Figs 1 and 2 (case 1) —Original observation

Figs 3 and 4 (case 1) —Observation three months later No quinacrine hydrochloride for four months

Figs 5 and 6 (case 2) —Original observation

Fig 7 (case 3) —Original observation



Center in June 1945, because of a light bluish pigmentation of the tip of the nose and inferior surfaces of the alae and a dark bluish gray discoloration of the hard palate (figs 5 and 6). The conjunctivas, scleras and cartilaginous portions of the ears, where ochronosis is likely to appear, were not affected. The soldier also had mild pigmentation of the nails of both little fingers and both great toes. The skin of the body generally showed to a mild degree the lemon yellow pigmentation characteristic of quinacrine.

This corporal had never taken quinine as a suppressive measure, however, he took quinacrine hydrochloride in a dosage of 10 to 14 tablets a week from the middle of October 1943 to the middle of May 1945, a period of nineteen months. He first noticed the pigmentation of the nose, just at the tip, about nine months prior to our seeing him, the spread to the inferior surfaces of the alae beginning about three months later. He did not know when the pigmentation of the palate occurred, but it was noted by a medical officer about five months prior to his visit to us.

He stated that during the time spent overseas, he had symptoms of malaria but was never treated or hospitalized for an acute attack.

No laboratory studies were carried out on this patient.

CASE 3—A sergeant in the Field Artillery, same division as the other two patients, aged 31, with four years and six months of service, with thirty-three months in the Southwest Pacific Area, was admitted to the hospital on March 29, 1945 for study, principally because of a vesicular eruption of both hands which had been present since December 1944. On physical examination, we noted a blue-gray, slate-colored discoloration of all the finger nails and toe nails. The location of the pigment seemed to be the same as in case 1, but the pigmentation itself was hardly as pronounced. The nails of the toes were more deeply pigmented than the nails of the fingers. The deposition of the pigment in the nail bed was of a diffuse character, and the transverse bands seen in case 1 were not present (fig 7). The skin of this soldier also showed deep yellow pigmentation characteristic of quinacrine.

This sergeant had never taken quinine as a suppressive measure. Quinacrine hydrochloride was taken for this purpose in a dosage of 10 to 14 tablets per week over a period of about sixteen months. He was not conscious of the discoloration of the nails until his return to the United States in March 1945, when he noticed it while on furlough at his home in Milwaukee. During his entire time overseas he suffered no illness whatever, other than the dermatitis involving both hands.

The same laboratory studies were performed in this case as in case 1, with results within a normal range.

The patient's course in the hospital was uneventful. The dermatitis, we felt, was on a contact basis, and with rest and symptomatic treatment the condition improved within a reasonable time, and he was discharged from the hospital.

We had an opportunity to see this patient again in July 1945, a little over three months after his original hospitalization. He reported to us that while at one of the reassignment centers he had his first malarial paroxysm and that smears of blood revealed *Plasmodium vivax*. For this attack, the patient was given quinacrine hydrochloride. At the time of this visit the dermatitis was causing little inconvenience. The pigmentation of the nails showed little change, other than possibly a slight fading.

In cases 4 to 8 the patients were young soldiers with mild to moderate pigmentation of some or all nails of the fingers and toes of the slate-colored variety observed in cases 1 and 3 and also the generalized lemon yellow pigmentation of

the skin characteristic of quinacrine. As previously stated, 3 of the patients belonged to the same division as the 3 previously reported. The other 2 were from a neighboring division with about the same length of service overseas and with a similar routine of suppressive quinacrine medication. Four of these 6 patients had had one or more attacks of *P. vivax* malaria. No detailed laboratory studies were done on any of this group.

#### COMMENT

We feel that the cases reported in this paper and the studies involved are of more than academic interest. The observations indicate that the pigment is located definitely not in the nail plate itself but in the bed of the nail. The exact nature of the pigment is certainly open to question, but its association with quinacrine therapy can hardly be doubted. It is significant that a decided fading of the pigmentation in case 1 (figs. 3 and 4) took place after the patient had been without the drug for about four months. This point was most encouraging, not only to the patient but to us because after this observation we were able to talk intelligently to the patients as to what might be expected in their particular cases. All the patients were stable persons, but all were to some degree concerned about their problem, especially the corporal with the striking nasal pigmentation. We made no definite promises to this group, but we were able to tell them that as a result of our observations in case 1 we felt that within a period of six to nine months the pigmentation probably would disappear. Another point worthy of consideration is the fact that 5 of this group of 8 are now civilians and may shortly consult their civilian physicians. If their physician is familiar with this problem, he in turn, can intelligently talk to his patient. One of the primary reasons for this report.

In considering the cause of pigmentation in these cases, the first question which arises is why a blue-gray color to the pigmentation is noted, in striking contrast to the lemon yellow hue of the usual quinacrine effect. A possible explanation was found in the excellent article of Jeghers on "Pigmentation of the Skin"<sup>11</sup>. It appears that, owing to the optical scattering phenomenon exhibited by the skin, deposits of pigment which are located in the corium, especially those in the dermal chromatophores, will give a gray to blue color clinically, depending on the amount and depth of the pigment. Numerous examples of this phenomenon can be cited, such as the blue nevus, Mongolian spots, argyria and the blue color produced by the black ink of tattoo artists. The single common factor in all seems to be the site of the deposition of the pigment.

In our cases the deposits of pigment below the thick nail plate were obviously located deep enough to cause the blue-gray color clinically. In case 2 we were unable to specify the location of the pigment.

but the similar color makes us believe that the pigment was deposited deep below the surface, probably in the cartilage

A further clue is found in the original observation of Virchow<sup>3</sup> in 1866 on ochronosis, a disease which he so named because of the yellow (ochre) granules which he found microscopically in the cartilage at post-mortem examination. This observation gives us a precedent for our conclusion in that a yellow pigment deposited below the skin clinically can produce a bluish discoloration.

Another factor to be considered is why such local depositions took place. It is reported that constipation, anemia and exhaustion from infectious disease augment the intensity and duration of the common yellow pigmentation due to quinacrine.<sup>4</sup> The importance of vitamins A and C and of nicotinic acid in pigmentation of the skin is well established.<sup>1b</sup> It is likely that the hardships of long service in the Southwest Pacific Area with its inevitable periods of malnutrition, the effect of the tropical sunshine, heat and humidity, together with the necessary but prolonged quinacrine suppressive therapy played a definite part in these cases. Perhaps under the influence of all these factors, including the high prolonged tissue saturation with quinacrine, the dermal chromatophores or tissue histiocytes, which have the property of phagocytosing pigments but not of producing them, were stimulated to seize on and fix the drug in these areas.

The third etiologic problem is that of the location of the pigment. Why the nail beds, the nose and the palate should be the only areas exhibiting these changes in our series of cases is a question to which we can offer no adequate answer. Trauma and the effects of sunlight<sup>4b</sup> could possibly be implicated so far as the nail beds and the nose are concerned, but the pigmentation of the palate as shown in case 2 cannot be explained on this basis. Again, the common yellow pigmentation is said to be more pronounced on the exposed body surfaces but staining of the mucous membranes has not been emphasized in the literature.<sup>4b</sup>

We feel that it is probable that this uncommon pigmentation reported in this paper is not as unusual as might be expected, since we were able to collect 8 cases within a relatively short time. It is also likely that in a larger series of cases similar deposits of pigment might be noted in other areas. We do not claim any priority in the observation of this condition because, at least in case 2 and probably in many more, a medical officer had already observed the discoloration.

3 Virchow, R. Ein Fall von allgemeines Ochronose der Knorpel und knorpelähnlichen Teile, *Virchows Arch f path Anat* 37 212, 1866.

4 (a) Schechter, A. J., and Taylor, H. M. Atabrine Pigmentation, *Am J M Sc* 192 645-650, 1936. (b) Soni, R. L. Note on Yellow Discoloration in Atabrine Therapy, *Indian M Gaz* 70-211-212, 1935.

The term "ochronosis" was intentionally avoided in the title because we felt it would only be confusing. As previously mentioned, the use of this term is usually limited to persons with alkaptonuria. In cases 1 and 3 alkaptonuria was ruled out by laboratory procedures, but because of the rarity of the condition tests to rule it out were deemed unnecessary in the other 6. Carbolochronosis<sup>5</sup> was ruled out in all cases by the history, for in none was there any evidence of the external use of phenol.

#### CONCLUSIONS

Eight cases of unusual pigmentation at uncommon sites, presumably due to quinacrine hydrochloride (atabrine), have been presented in order to familiarize not only army medical officers but civilian physicians as well with the existence of such a condition. We have discussed various etiologic factors which may have been implicated in the development of this pigmentation. It is our impression that the pigmentation has no permanent untoward effect and that after withdrawal of the drug it should disappear within a period of six to nine months. The problem has been presented in no way to cast disfavor on quinacrine, because those of us who have been confronted with malaria in the army know that the drug has served us well.

Captain Jean Pilot, Medical Corps, Army of the United States, Chief of the Laboratory Service, Regional Station Hospital, Fort Sheridan, Ill., took the original Kodachromes. T/5 William McHugh Jr., Photographer, Gardiner General Hospital, assisted in copying.

5 Fishberg, E. H. Ueber die Carbolochronose, *Virchows Arch f path Anat* **251** 376-418, 1924.

# IMMUNIZATION THERAPY FOR LICHEN PLANUS

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THE cause of lichen planus is still unknown, but various theories regarding it have been advanced. They include the nervous, the infectious, including the focal infectious, the toxemic and the constitutional diathetic theory. Lichen planus has also been called a syndrome, thus, of course, concedes a possible causal importance to all the factors mentioned and allows the inclusion of the lichen-planus-like toxicodermas. All these theories have been comprehensively discussed by F Juliusberg.<sup>1</sup>

The experiments reported in this paper are based on the infectious theory, which is supported by certain clinical and experimental experiences, by certain therapeutic reactions and by observations which suggest contagiousness. The necessity of keeping this paper as short as possible prevents us from entering into a more detailed discussion of these and related factors with reference to the literature concerned.

Extending full consideration to the other hypotheses mentioned, one of us (Biberstein) believes that the theory of infection as the cause of lichen planus, advanced by Hallopeau<sup>2</sup> and Jadassohn,<sup>3</sup> is the most probable one and that a virus may be the cause, as suggested by Darier,<sup>4</sup> Lipschutz,<sup>5</sup> Klaar and Rosner<sup>6</sup> and Kogoj.<sup>7</sup>

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1 Juliusberg, F. Lichen ruber und Pityriasis rubra pilaris, in Jadassohn, J. Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol 7, pt 2, p 1

2 Hallopeau, H, cited by Jadassohn<sup>3</sup>

3 Jadassohn, J. Beiträge zur Kenntnis des Lichen, nebst einigen Bemerkungen zur Arsenotherapie, in Festschrift gewidmet Moriz Kaposi zum funfundzwanzig-jährigen Professorenjubiläum, Vienna, 1900, p 877

4 Darier, J, cited by Juliusberg<sup>1</sup>

5 Lipschutz, B, cited by Juliusberg<sup>1</sup>

6 Klaar, J, and Rosner, R. Zur Frage der Lichen-ruberartigen Salvarsan-exantheme und Psoriasis vulgaris nach Salvarsandermatitis, Dermat Ztschr 42: 127, 1924

7 Kogoj, F. L'etologie du lichen plan, Zentralbl f Haut- u Geschlechtskr 25: 417, 1928

Based on experience with immunizing therapy for verruca vulgaris, verruca plana and condyloma acuminatum in man<sup>8</sup> and papillomatosis in cows and horses,<sup>9</sup> Biberstein also tried an immunization therapy for lichen planus. The first positive results of treatment in 9 of 13 cases in which this treatment was used (to which 2 with successful treatment were later added) have been mentioned in a previous paper<sup>8b</sup>

#### PREPARATION AND ADMINISTRATION OF LICHEN PLANUS ANTIGEN

The antigen for the treatment of lichen planus was prepared as follows from lichen planus tissue in which the virus was assumed to be present

Papular or hypertrophic lesions, cleansed with alcohol and ether, were anesthetized with procaine hydrochloride and epinephrine hydrochloride by subcutaneous injection and removed with a sharp spoon or a curet. The borders between the lichen planus infiltration and the normal tissue of the cutis were easily felt, so that any deeper injury to the cutis was avoided. The erosions healed within ten to fourteen days with use of a mild salve (e.g., boric acid ointment or bismuth subgallate-zinc oxide paste)

The scrapings were cut into small pieces with scissors and ground in a mortar with isotonic solution of sodium chloride until a pulp resulted. Approximately 3 parts of the solution was added to 1 part of solid particles. This slush was kept at room temperature for twenty-four hours and then placed into a water bath at a temperature of 56 to 60 C for sterilization for two hours. After bacteriologic sterility tests in liquid and on solid mediums did not show any growth, the suspension was filtered through sterile gauze in order to remove particles which would not pass through a needle. Phenol was added as a preservative (0.5 per cent)

As explained in a previous paper,<sup>10</sup> this procedure seems sufficient to kill the hypothetical virus, and from the use of an antigen as described we have yet to observe any effect which could be ascribed to the inoculation of a still virulent germ or virus

The antigen thus prepared was administered intracutaneously twice weekly, two injections, 0.1 cc each, were given at each treatment. This dosage was based on experience published in a previous paper (Biberstein and Oschinsky<sup>11</sup>)

#### PATIENTS TREATED IN THIS SERIES

We have treated 40 patients: 25 boys and men, 17 to 74 years old, and 15 women, 29 to 70 years old. The duration of the disease in these patients, as far

8 Biberstein, H. (a) *Versuche ueber Immuntherapie der Warzen und Kondylome*, *Klin Wchnschr* **4** 638, 1925, (b) *Die Immuntherapie der Warzen und Kondylome*, *ibid* **11** 1021, 1932, (c) *Immuntherapie der Warzen und Kondylome bei Mensch und Tier*, *Tr Internat Dermat Cong* (1930), 1931, p. 711

9 Biberstein, H., and Suessenbach, E. *Therapie der Hautpapillomatose des Rindes*, *Tieraerztl Rundschau* **38** 60, 1931

10 Biberstein, H. *Immunization Therapy of Warts*, *Arch Dermat & Syph* **50** 12 (July) 1944

11 Biberstein, H., and Oschinsky, F. *Versuche ueber die Empfindlichkeit der menschlichen Haut gegen Tiersera*, *Arch f Dermat u Syph* **142** 353, 1923



as could be ascertained, was from three months to eighteen years, with the exception of 1 patient, a woman 70 years old, whose eruption had begun three months previously, who told us that forty years before she had had the same disease, which was successfully treated with arsenic

#### CLINICAL VARIETIES TREATED

Twenty-eight patients showed the typical picture of lichen planus, many of them with eruptions spreading widely over the body and extremities others with manifestations on more limited areas or with a discrete distribution on the trunk and extremities Each of 3 patients had exanthem with so many follicular lesions, many of them in corymbiform arrangement, that the eruption was called lichen planus et follicularis Seven patients showed a definite tendency for many or all of their lesions to become hyperkeratotic, so that their eruptions were designated as lichen planus hypertrophicus One patient had many bullous lesions in an exanthem which otherwise was lichen planus One patient showed patchlike lesions of lichen planus limited to the buccal mucosa (see Fox,<sup>12</sup> in his discussion of a demonstration by Scheer) as remnants of a former widely disseminated lichen planus of eleven years' duration

#### RESULTS

Of the 40 patients treated 7 were lost from observation, for the most part after insufficient or irregular treatment Two of them (after nine and thirteen injections) had exhibited signs of improvement (diminished pruritus or flattening of the lesions), 4 others, some of them at irregular intervals, had received one, five, seven and eight treatments and 1 additional patient had been treated fourteen times within sixty-three days and, after an interval of four months, eleven times within ninety-one days

Of the remaining 33 patients, 3 did not respond to treatment The first, a man aged 53, had had lichen planus for eighteen years During this time, he had been treated without benefit with roentgen rays, cresol, a bismuth preparation, arsenic and a salve containing radium emanation He did not respond to forty-seven injections of our stock antigen or to injections of an autoantigen Another male patient with lichen planus of three months' duration had not responded to ten injections of a bismuth preparation and did not react to sixteen injections of our stock antigen or to ten of an autoantigen Subsequently he took drops of arsenic for one month, and five months later the eruption on the thighs, legs and feet began to recede Six months after this the remaining areas of the trunk were treated with roentgen rays, resulting in the disappearance, without pigmentation, of all the lesions except for one patch on the back This resistant area, larger than the size of one's palm and its elements, which have not yet been examined histologically, show a peculiar pinkish color and resemble closely a xanthoma The third failure occurred in a man 47 years old

<sup>12</sup> Fox, H. in discussion on Scheer, M. Lichen Planus of the Mouth, Arch Dermat & Syph 19 693 (April) 1929

who during the past six years had been treated repeatedly for recurring lichen planus with mercury salicylarsenate, mercury bichloride and a bismuth preparation. He received fourteen injections of an antigen within fifty-eight days without showing any sign of a reaction.

The treatment of the remaining 30 patients gave the following results:

*Group I*—Sixteen patients (9 men and 7 women) were clinically cured. No lesion remained.<sup>13</sup> Thirteen of them had had lichen planus for less than one year and 3 for one year or more (1 of these for more than two years and 1 for more than ten years).

*Group II*—Eight patients (4 men and 4 women) had widely disseminated eruptions and numerous lesions which cleared up, except for one or a few isolated groups of lesions, so that most of these patients considered themselves cured.<sup>14</sup> The duration of the disease in this group was less than one year in 6 patients (including the aforementioned ones who had had lichen planus forty years ago) and one year or slightly longer in 2 patients.

*Group III*—Six patients (4 men and 2 women) showed considerable improvement by the healing of large areas, several larger patchlike groups of lichen planus, however, retained their original size, sometimes confined to definite regions as described later, responding to continued treatment only slowly, if at all. The duration of the disease prior to our treatment was less than one year in 2 cases, one year in 1 case and more than one year in 3 cases.

Summarizing, we can say that of the 33 patients treated and observed over a reasonably long time 3 did not respond, 16 were completely cured, 8 were cured with a remnant and 6 were considerably improved.

#### SPECIAL FEATURES

Some observations made during the course of this investigation merit special discussion.

*The Course of the Disease under Treatment*—Diminution of the pruritus, ending in complete cessation of it, was usually the first result noticed by the patient. This diminished rather suddenly, and then the lesions began to pale and to flatten, occasionally accompanied with exfoliation of thin scales, until the lesions completely disappeared without leaving a trace. In larger patches, the tendency to superficial scaling manifested itself by the formation of cigaret-paper-like pleating of the uppermost epidermal layers, this, however, did not end in atrophy but was exfoliated without sequelae. This superficial peeling was greatest in the patient with the bullous type of the disease.

13 One patient treated by Dr. C. K. Good.

14 One patient treated by Dr. E. Rosenbaum.

In those patients in whom the follicular corymbiform lesions were predominant, the tiny follicular hyperkeratoses proved to be especially persistent. Many of them were still palpable when they could not be seen with the naked eye. In many patients, including those who had not been treated with arsenic, pigmentation accompanied the flattening of the lesions, and in some patients it outlasted for many months the disappearance of the itching and the papules. Treatment with the antigen, continued after the disappearance of the other subjective and objective symptoms, did not seem to accelerate the disappearance of the pigmentation.

In some cases, improvement did not start uniformly in all the involved areas but, corresponding to the observations of Kogoj,<sup>15</sup> started on the trunk and upper extremities. This was most conspicuous in a patient with a generalized, partly corymbiform, follicular lichen planus in whom the numerous lesions on the trunk and the arms disappeared within the usual period, while the eruption on the legs proved to be most resistant. Although slow improvement occurred, the eruption still was present after injections of stock antigen and autoantigen, some of them given into the lesion or, at least, into the most involved areas. In other cases, the lesions on the abdominal wall or the submammary regions responded more slowly than those on the arms. However, in 1 patient with a successfully treated generalized eruption, the improvement began on the legs.

As previously observed in studies on warts and condyloma acuminatum, the treatment may result in cure, except for one or a few groups of lesions, which sometimes respond to a prolonged treatment. In one such instance, with half-dollar-sized rest patches on both thighs, treatment was resumed after an interval of five months. One patch disappeared after twelve more injections, the other decreased in size and was clinically cured after forty treatments. This patient is classified in group II.

Other such patients had remnants that proved to be definitely resistant, at least as long as the treatment continued. One patient, examined two years after cessation of treatment, showed a small remnant unchanged, however, there was no new dissemination. In 1 case, we removed the remnant with a curet. We cannot give any explanation for the remnants, but as far as we can ascertain, they have nothing to do with primary lesions.

Lichen planus of mucous membranes proved to be more resistant than that of the skin also under the immunizing treatment. In 1 patient with almost thumbnail-sized patches on both buccal mucosae larger parts of them seemed to peel off after the seventh treatment,

<sup>15</sup> Kogoj, F. Ueber die Aetiologie des Lichen ruber planus, *Med Pregl* 3:140, 1926, abstracted, *Zentralbl f Haut- u Geschlechtskr* 31:472, 1929.

leaving redness but no erosions, and after the fourteenth treatment the major part of the patch had disappeared. This patient is classified in group III. In a patient in group II the extensive involvement of the tongue began to clear in irregularly bordered patches after twelve injections, while the typical lichen planus pattern on the buccal mucosa did not improve, the latter began to clear after a total of forty injections.

Two patients (1 with lichen planus et follicularis, and 1 with lichen planus resembling lichen nitidus) had psoriasis at the same time, both reacted to the antigen with complete disappearance of their lichen planus, but the lesions of psoriasis were entirely unaffected.

*The Number of Treatments and the Period of Time*—The number of treatments necessary until the beginning of an effect, usually the cessation of itching, varied between 4 and 13 in all groups, an average of 8 to 9. Ten of the 16 patients of group I needed 8 to 10 treatments before definite improvement could be recognized. The figures for groups II and III, which required about the same average treatment, are too small to permit the computing of a definite average. The period of time necessary until the first reaction became recognizable was 33.6 days in the first group, 41.7 days in the second and 39.1 days in the third. Since the average number of treatments is approximately the same for all three groups, the difference in the time between group I and groups II and III indicates that in the latter groups the patients came for treatments irregularly almost from the beginning. This may explain some of the observed resistance described subsequently. We must concede, however, that 1 of the 3 patients who did not react at all was conscientious about appearing for treatment.

The number of treatments necessary for the eventual result was five to twenty-seven for 15 patients of group I and forty-nine for the sixteenth (with lichen planus et follicularis of more than ten years' duration). Therefore the average number of treatments necessary for a definite clinical cure was 18.69 for this group and, if the sixteenth case is considered as an exception, only 16. For group II the average number of treatments was 24.6. This figure is probably too high, since if in the course of treatment some groups did not continue to improve it was difficult to determine the time at which no further progress toward healing was made. Consequently, more injections were given beyond that point in vain. The same is true for group III, in which we averaged 25.6 injections before we were convinced that no further progress could be made.

The total length of the period of treatment was thirty-one to one hundred and eleven days for 15 patients of group I and two hundred and nine days for the sixteenth, who required exceptionally long treatment. This is an over-all average of 76.5 days and, without the sixteenth unusual case, 67.4 days. The corresponding figures for groups II and

III, i e, the time in which the injections did not accomplish any further improvement, are 1472 and 1226 days of treatment, the difference between the two groups probably has little importance, since it may be due to the low figures present in these groups

We cannot state definitely how long treatment should be continued. In order to prevent recurrences it seems advisable to continue the injections for four to six weeks after the cutaneous manifestations have disappeared. The pigmentation resulting in some cases does not seem an indication for continuing therapy, in examining patients who had been successfully treated eighteen months previously, we found remnants of pigmentation without formation of lichen planus papules or complaint of itching. In 3 patients for whom treatment was continued for many weeks after the papules had entirely disappeared and only pigmentation remained, the pigmentation faded just as slowly as if no further treatment had been given.

It cannot be foretold whether lichen planus will heal with or without pigmentation or how long pigmentation will remain.

The prolonged treatment, rather than the initial part of the treatment, for groups II and III was often more irregular than for group I. This points to the possibility that irregularity of treatment may be a contributing factor to the unsatisfactory result. This possibility is supported by observations which will be discussed later.

*Recurrences* (a) *Recurrences Following Apparently Sufficient Treatment* One case of this kind was observed, arms and buttocks and flexor surfaces of the legs and the ankles of the patient were involved initially. After eight treatments improvement was noted, and after nineteen treatments all the lesions had disappeared, leaving pigmentation. The patient was discharged after twenty-two injections, on the fifty-fourth day. Examination four months later did not reveal any lesions, except for remnants of pigmentation. Two months later, the patient had four lichen planus papules, which disappeared after three injections. Thirteen months later, she was free from any eruption.

(b) *Recurrences Following Premature Discontinuation of the Treatment* For the time being, we consider fifteen injections as a minimum treatment, because 10 of the 16 cured patients required fifteen injections or less. Therefore, we are inclined to consider the close of a course of treatment as premature if less than fifteen injections have been given, which, of course, does not necessarily mean that a patient cannot be cured with less than that number.

A patient, 44 years old, with lichen planus of the glans and shaft of the penis had been unsuccessfully treated with sulfathiazole elsewhere. After four days of medication with arsenic he had abdominal cramps, and therefore we decided to use injections of an antigen. Since relief from the "terrific" itching could not be expected for four to five weeks, according to our experience, he received 80

roentgen rays filtered through 0.5 mm of aluminum to the dorsal surface of the shaft of the penis. After four such irradiations and five injections of an antigen, which were given between June 5 and July 12, the papules and the itching had disappeared, and therefore the patient discontinued treatment. On August 26, he returned with a recurrence on the glans penis, but after four injections the lesions faded and disappeared. He continued irregularly with treatment, receiving only four injections until October 11. No roentgen ray therapy or other form of treatment was given besides the injections of an antigen. In March of the following year, he returned with herpes simplex of the sulcus coronarius, which healed with the application of a 5 per cent bismuth subgallate-zinc oxide paste, and numerous lichen planus lesions on his glans. They disappeared after four injections of an antigen given within two weeks, this time, treatment consisted of fifteen injections given within sixty days.

In this case there was a tendency for the eruption to recur after insufficient injections had been given over an extended period of time. It is probable that during the first phase the favorable effect was due to the antigen and not to the roentgen rays and that in this case the roentgen rays apparently affected neither the course nor the symptoms of the lichen planus.

#### (c) Recurrences Following Initial Improvement After or During Irregular Treatment

A man aged 56 classed in group III, had had lichen planus with many annular lesions for about one year. Since he had not responded to five injections of a bismuth preparation, he was treated with an antigen for lichen planus. After four injections, given within two weeks, itching disappeared, and the lesions showed definite involution with scaling. Then the patient came in irregularly and received the next five injections within forty-nine days, one injection about every tenth day instead of every third or fourth day. Nevertheless, the majority of the lesions became flattened, and some pigmentation was present with involution most evident in the center of some of the patches. The next four injections were given within seven weeks, and at the end of that time two papular groups were left. During the following one hundred and five days he was treated twelve times, and after that one group was left on the dorsum of one hand. He came for treatment twenty-four times at irregular intervals within the following two hundred and eighty days. The papular group on the hand never disappeared, and, from time to time, small lesions appeared until, about five weeks after the two hundred and eighty day period, a considerable eruption of lichen planus appeared on the trunk, the arms and the legs. From this time, the patient appeared for treatment regularly twice a week. The eruption on the trunk and the arms responded comparatively quickly, while the partly hypertrophic eruption on the legs proved more resistant.

In group II, a woman, aged 49, had had lichen planus of the wrists, and arms and in the submammary regions for about one year. After eight treatments had been given within five weeks, the itching disappeared and the patient began to report for treatment irregularly, not even as often as once a week. On the seventy-eighth day of treatment, several new lesions appeared, whereupon the patient came regularly for one month but only seven times during the following two months. After a total of thirty injections her arms were practically free of lesions, while the submammary region showed fewer lesions. From July to the following March,

she received forty-four injections at the rate of five injections monthly, given at irregular intervals. Except for a few papules, when the patient was last treated, the entire eruption had disappeared, leaving pigmentation.

In a patient treated by Dr Ernst Rosenbaum with an autoantigen made by us, a generalized lichen planus which had not responded to oral medication with arsenic began to respond after ten injections of the antigen and was greatly improved after the twentieth injection, given within eighty-one days. The patient then began to come for treatment irregularly, so that she received only six additional treatments within fifty-four days. She was cured, except for insignificant remnants, when she discontinued treatment, but, according to a report which Dr Rosenbaum received from another physician, a slight recurrence, not seen by Dr Rosenbaum, disappeared after tonsillectomy.

One or more patients of groups II and III could be discussed here, but the examples cited seem to show that the scattering of the doses, by prolonging the intervals and irregularity of the intervals, encourages recurrences. This holds true as well for cases which reacted favorably at the beginning of the treatment. In addition, although we promptly succeeded in curing both relapses in the case described which recurred after premature discontinuation of treatment and effected improvement in 2 cases just described, the scattering of the doses seems to impair or weaken the effect of the antigen more than premature termination of the course of therapy does.

#### COMMENT

In evaluating the result of any therapy for lichen planus, one must consider the fact that the normal course of lichen planus varies greatly and that during the course of its spontaneous involution it may undergo roughly the same changes as those observed during its response to therapy. As in many other diseases which show spontaneous remissions and even cures, these facts have not deterred investigators from therapeutic experiments with lichen planus. The procedure used by us is but one more effort in this field.

The number of patients treated is still small. We should appreciate it if other investigators would use the antigen treatment so that its value may be further demonstrated.

#### SUMMARY

As a basis for an immunization therapy of lichen planus the hypothesis is assumed that lichen planus is caused by an infectious agent which is present, at least at times, in the lesions.

This hypothesis is based on the clinical features of the disease, their development, the effects of therapy and the nosologic or epidemiologic observations including post-traumatic eruptions, geographic factors and familial occurrence. Based on the hypothesis mentioned, an

immunization therapy had previously been inaugurated by one of us (Biberstein) and successfully tried in a small number of cases. We have continued these investigations on a broader scale.

An extract made from lichen planus lesions was used as the antigen, its production and administration have been described.

This immunization therapy was applied to 40 patients, many of them previously treated by other methods with unsatisfactory results. Seven of them discontinued treatment prematurely, so, a conclusion cannot be drawn regarding them. Of the remaining 33 patients, 3 were not benefited, 6 improved considerably, 8 were practically cured, retaining only insignificant remnants which cannot be explained, and 16 were completely cured clinically. Altogether, 30 of the 33 patients who could be followed up were favorably influenced.

The course of the process of healing is described.

Fifteen to twenty double injections given semiweekly are considered to be sufficient for treatment in the majority of cases in which there is a reaction. Premature termination of treatment encourages recurrence. Scattering of the doses and irregularity of the intervals are detrimental to the efficiency of the antigen, favoring relapse. One occurrence, however, was observed following treatment which had been continued beyond the time of the disappearance of the eruption.

#### CONCLUSIONS

1 Lichen planus and all its variations can be influenced in a high percentage of cases by immunization therapy.

2 The results of our investigations support the hypothesis of an infectious origin for lichen planus.

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## EPIDERMAL SENSITIVITY TO PENICILLIN

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IN A previous study <sup>1</sup> we reported the results obtained by means of a penicillin ointment in the treatment of 48 patients with pyogenic infections of the skin. Most of the cutaneous infections were cured or improved, but a contact dermatitis developed in 5 of these patients during treatment. Of these 5 patients 2 were available for patch tests. Positive reactions to patch tests were obtained only with commercial penicillin sodium, indicating that penicillin sodium was responsible for the sensitivity in these cases. The present work was undertaken to determine whether or not persons could be sensitized to the penicillin ointment and what ingredient of the ointment was responsible for the sensitivity.

Contact dermatitis has been reported in persons who handle the salts of penicillin. Applying test patches to some of them has revealed that the sensitivity may be due to penicillin salts.

Pyle and Rattner <sup>2</sup> reported the first case of contact dermatitis due to penicillin in a medical officer who prepared solutions of penicillin. A positive reaction to a patch test with the penicillin was observed in this case. Silvers <sup>3</sup> administered patch tests to a chemist in whom contact dermatitis had developed while he was handling amorphous sodium penicillin. Patch tests elicited positive reactions to the "impure" yellow amorphous sodium penicillin and negative reactions to pure white crystalline sodium penicillin. Binkley and Brockmole <sup>4</sup> observed

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1. Gottschalk, H. R., Engman, M. F., Jr., Moore, M., and Weiss, R. S. Penicillin Ointment in Some Infections of the Skin, *Arch. Dermat. & Syph.* **53**:226 (March) 1946.

2. Pyle, H. D., and Rattner, H. Contact Dermatitis from Penicillin, *J. A. M. A.* **125**:903 (July 29) 1944.

3. Silvers, S. H. Contact Dermatitis from Amorphous Sodium Penicillin, *Arch. Dermat. & Syph.* **50**:328 (Nov.) 1944.

4. Binkley, G. W., and Brockmole, A. Dermatitis from Penicillin, *Arch. Dermat. & Syph.* **50**:326 (Nov.) 1944.

two physicians with contact dermatitis from penicillin. Patch tests with penicillin sodium dissolved in isotonic solution of sodium chloride elicited positive reactions in 1 patient and not in the second. Parenteral administration of penicillin to the second was followed by a papular eruption of the hands and feet.

Some investigators who have applied penicillin locally have reported instances of contact dermatitis developing during treatment. Patch tests were used for additional information by two of these investigators. Roxburgh<sup>5</sup> treated 75 patients with pyogenic infections of the skin with local application of penicillin. He stated that in 2 of his patients penicillin ointment appeared to be irritating to the skin. One hundred patients with infections of the skin were treated with penicillin administered locally and parenterally by Cohen and Pfaff.<sup>6</sup> They found that 4 presented an acute reaction to the drug after application. Cohen and Pfaff administered patch tests with the ointment and found that 0.95 per cent of 524 patients had positive reactions to it. They did not determine to what single ingredient of the ointment these patients were sensitive. Of the 94 patients who were treated by Wrong,<sup>7</sup> in 2 acute inflammations developed in the areas where penicillin ointment had been applied. This inflammation was thought to be due to penicillin because positive reactions to patch tests were obtained to "penicillin emulsion" but not to the "emulsion" itself.

#### THE OINTMENT

The penicillin ointment that was used for the patches was the same ointment used for the clinical trials. It was made with sterile materials under aseptic conditions. The ointment base was water-miscible and contained glyceryl monostearate, stearic acid (U S P), Duponol, a preservative and refined peanut oil and distilled water. The  $pH$  was approximately 6.5. Commercial penicillin sodium which had been pretested by the United States Food and Drug Administration was added in a concentration of 500 Oxford units per gram.

#### PROCEDURE OF ADMINISTERING PATCH TESTS

The patch tests with the penicillin ointment were performed according to the procedure recommended by Dr. Louis Schwartz and Dr. Samuel M. Peck.<sup>8</sup>

A group of 200 volunteers were tested. These volunteers were factory employees and patients at two of the St. Louis hospitals. The ages of the volunteers ranged from 16 to 70, the average age being 39. There were 66 males and 134 females. Three of the volunteers were Negroes and the remaining volunteers, white.

<sup>5</sup> Roxburgh, I. A., Christie, R. V., and Roxburgh, A. C. Penicillin in Treatment of Certain Diseases of the Skin, *Brit. M. J.* **1**: 524 (April 15) 1944.

<sup>6</sup> Cohen, T. M., and Pfaff, R. O. Penicillin in Dermatologic Therapy, *Arch. Dermat. & Syph.* **51**: 172 (March) 1945.

<sup>7</sup> Wrong, N. M. Penicillin Therapy in Skin Infections, *Canad. M. A. J.* **52**: 341 (April) 1945.

<sup>8</sup> Schwartz, L., and Peck, S. M. The Patch Test in Contact Dermatitis, *Pub. Health Rep.* **59**: 546 (April 28) 1944.

The technic employed was as follows (see tables for details of results)

1 The penicillin ointment and the ointment base as a control were applied to pieces of gauze  $\frac{1}{4}$  inch (0.6 cm) square and covered with standard Elastopatch (Duke Manufacturing Company)

2 The patches were placed on the skin of the back or the legs or the arms

3 The patches were removed approximately forty-eight hours later and the areas observed. The areas were again observed in ninety-six and one hundred and ten hours

4 When ten or more days had elapsed after the removal of the first patches, the patches were reapplied and steps 2 and 3 repeated

All subjects who reacted positively to the penicillin ointment were given patch tests with commercial penicillin sodium dissolved in isotonic solution of sodium chloride (10,000 units per cubic centimeter). This penicillin solution was placed on cotton and covered with rolled-up finger cots so that as little evaporation as possible would take place. Isotonic solution of sodium chloride applied in the same manner was used as a control.

An extract of *Penicillium notatum* was prepared and used to test all volunteers who had had positive reactions to the ointment. The extract was made by washing the growth of *P. notatum* with sterile isotonic solution of sodium chloride three times<sup>9</sup>. The fungus was then dried and extracted with acetone. This extract was then concentrated to make an approximate 25 per cent solution in acetone. Acetone was used as a control in these patch tests.

# RESULTS

The cases of 9 of the volunteers (table 1) were not included in the final tabulation of the 200 cases, because subsequent investigation

TABLE 1—*Reactions to Patch Tests of Patients with History of Contact with Penicillin*

Case	Sex	Ointment Plus Penicillin	Ointment Base	Penicillin Sodium, Cup	Extract of Penicillium
1	M	2+*	1+	1+	0
	(Had received injections of penicillin)				
2	F	1+	0	0	0
3	F	2+	0	0	0
4	M	2+	0	0	
5	M	3+	0	3+	
6	M	3+	0	1+	0
7	M	3+	0	3+	
8	M	1+	0	0	0
9	M	1+	0	0	
	(Had received 666,000 units of penicillin by injection)				
Positive reactions		8	1	4	0

\* 1+, erythema, 2+, erythema and edema, 3+, erythema, papules and a few vesicles, 4+, erythema, edema, many vesicles and, in some cases, ulceration

revealed that these volunteers either had received penicillin parenterally or had had prolonged contact with the penicillin salts. The results for

9 This extract was prepared by Dr. Morris Moore, mycologist to the Barnard Free Skin and Cancer Hospital

these 9 volunteers are of some interest. Of the 2 volunteers who had received injections of penicillin 1 reacted positively to the patch test with the penicillin ointment, and 1 did not. Of the 7 volunteers who had had prolonged contact with penicillin, 7 reacted to the ointment containing penicillin and none reacted to the ointment base. In 4 of the 9 volunteers positive reactions to patches with penicillin sodium were obtained. None of the 5 volunteers tested reacted to the extract of *Penicillium*. Three of the persons who had had prolonged contact with penicillin were given 100 units of penicillin sodium dissolved in isotonic solution of sodium chloride subcutaneously in the right arm. No reac-

TABLE 2—*Reactions to First Patch Tests of Patients with No Previous Contact to Penicillin*

Case	Sex	Ointment Plus Penicillin	Ointment Base	Penicillin Sodium, Cup	Extract of <i>Penicillium</i>
1	F	1+	0	0	0
2	F	2+	2+	0	
3	F	2+	0	0	0
4	M	1+	1+	0	
5	F	1+	1+	0	
6	M	1+	0	0	
7	F	1+	0	0	
8	F	1+	1+	0	
9	M	1+	0	0	0
10	M	1+	0	0	
11	F	1+	0	0	
12	F	2+	0	0	
13	M	2+	0	13+	
14	F	1+	1+	4+	
15	M	2+	0	3+	0
16	M	1+	0	1+	
17	M	2+	0	3+	0
18	M	2+	1+	1+	
19	M	1+	0	1+	
20	M	2+	1+	1+	
21	M	1+	0	3+	0
22	M	3+	0	3+	0
23	M	4+	0	1+	
24	F	2+	1+	0	
Positive reactions		24	8	11	0

tions, either local or general, were observed after this subcutaneous injection, although 1 of these persons had had a positive reaction to the patch test with penicillin sodium.

Twenty-four volunteers (table 2) who had had no previous contact with penicillin as far as we could discover demonstrated positive reactions to the patches with penicillin ointment on the first testing. Of these 24 volunteers, 8 reacted to the ointment base and 11 reacted positively to the penicillin sodium dissolved in isotonic solution of sodium chloride. None of these volunteers reacted to the extract of *Penicillium*. In general the reactions to the base were somewhat less severe than those to the base plus the penicillin. Although none of these volunteers gave a history of previous contact with penicillin, many of them appeared to be sensitive to penicillin sodium.

At the second testing 17 volunteers (table 3) had positive reactions to patch tests with the penicillin ointment. Eight of these volunteers reacted to the ointment base but with only 1 plus reactions. Only 1 of the volunteers reacted to penicillin sodium, and the same person reacted slightly to the extract of *Penicillium*. It would appear that we had sensitized at least 11 persons to the penicillin ointment and at least 8 to the ointment base. We were apparently successful in sensitizing 1 to penicillin sodium.

TABLE 3—*Reactions to Second Patch Tests of Patients with No Previous Contact to Penicillin*

Case	Sex	Ointment Plus Penicillin	Ointment Base	Penicillin Sodium, Cup	Extract of <i>Penicillium</i>
1	F	2+	0	2+	1+
2	F	1+	0	0	
3	F	1+	1+	0	
4	F	1+	0	0	
5	F	1+	0	0	
6	F	1+	1+	0	
			(on first patch test 1+ to base)	1+	
7	F	2+	1+	0	
8	F	1+	0	0	
9	M	1+	0	0	
10	F	2+	1+	0	
11	F	1+	0	0	
12	M	2+	0	0	0
13	F	1+	0	0	
14	F	1+	1+	0	
15	F	1+	1+	0	0
			(on first patch test 1+ to base)	1+	
16	F	1+	1+	0	0
17	F	1+	1+	0	0
Positive reactions		17	8	1	1

The penicillin ointment in the concentration used in this study is apparently not a primary irritant, as not all of those tested reacted to it.

#### COMMENT

Of 7 persons who had had prolonged contact with penicillin sodium 7 were sensitive to the patch tests with penicillin ointment and none to the tests with the ointment base. Three reacted to penicillin sodium dissolved in isotonic solution of sodium chloride on test patches. These volunteers had apparently become sensitized to penicillin through their contact with it. Study of the literature revealed that persons who had worked with penicillin might become sensitized to it, and our results seem to confirm this observation.

The positive reactions to the first patch tests with penicillin ointment are more difficult to explain. The 24 volunteers who were sensitive had had no contact with penicillin that we could discover. However, 11 of them reacted to penicillin sodium when patch tests were performed with it. This might indicate that the reason for the reaction to the ointment was a sensitivity to penicillin sodium at that time. It is known that many persons are sensitive to the antigen of the *Penicillium* family. Feinberg<sup>10</sup> demonstrated that such persons would not necessarily be sensitive to penicillin. He used patients who were clinically sensitive to the *Penicillium* mold and did not find positive reactions to scratch tests with penicillin in these patients. Since we worked with patch tests, our results are not entirely comparable with his. It is possible that persons who are sensitive to the *Penicillium* mold may show positive reactions to patch tests with penicillin sodium. We did not perform scratch tests with extracts of the mold on any of our volunteers, but we used patch tests instead. We observed only one positive reaction to patch tests with extract of *Penicillium* in persons who reacted to the ointment. Another explanation for the positive reactions to penicillin sodium may be that we sensitized these persons to penicillin sodium by the previous patches with the ointment. This could have happened, but it would not explain the original positive reactions to the penicillin ointment.

The second testing with the penicillin ointment demonstrated that the substance is evidently a sensitizer with some degree of potency, as we found that 17 persons reacted to the second tests when they had not reacted to the first. The reactions were apparently due to the penicillin sodium in 9 of the 17, since these 9 did not react to the base. We were not able to prove this with certainty, as only 1 of these 9 gave positive reactions to the patch tests with the penicillin sodium.

#### CONCLUSIONS

Penicillin when used locally is capable of producing contact reactions, sometimes severe, in an unknown percentage of the population.

Penicillin, apparently, is not a primary irritant in the concentration employed in these studies.

By means of patch tests we were able to produce epidermal sensitization to a penicillin ointment in 4.5 per cent of 200 persons.

We did not have enough material to determine whether epidermal sensitization predisposed to dermal or vascular sensitization. What little evidence we have indicates that this is not the case.

For the present, not too much reliance should be placed on the results obtained in 200 to 300 persons.

10 Feinberg, S. M. Penicillin Allergy, *J. Allergy* **15** 271 (July) 1944.

*GOTTSCHALK-WEISS—SENSITIVITY TO*

The procedure recommended by Schwartz and I<sup>1</sup> is out, but whether or not these results are statistical to question. Our definite positive results would indicate that a percentage of the population is primarily sensitive to penicillin, and another smaller percentage can be sensitized to penicillin by repeated injection to the skin over a period of five to ten days.

Much more work must be done before absolute results can be obtained, but, in the meantime, we believe that there is no contraindication to well controlled experimental use of penicillin, providing the patients are followed carefully and observed for allergic reaction.

## MICROPAPULAR TUBERCULID IN THE NEGRO

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NEW YORK

MICROPAPULAR tuberculid is rather common in Negroes but less so than papulonecrotic tuberculid. Many cases escape detection because of the frequent sparseness of the eruption and also because the microscopic picture may prove misleading. In my experience the majority of patients exhibit a scanty type of eruption, but lesions may be profuse enough to involve the entire body.

The eruption usually makes its appearance first on the face and may be confined entirely to this area, but there is a tendency to generalization and lesions have been noted everywhere on the cutaneous surface, except on the palms and soles and in the oral cavity. On the extremities there is a predilection for the extensor surfaces. Involvement of the scalp is not uncommon, the lesions being most numerous on the perimeter and possibly confined exclusively to the margins. The vermilion border of the lips, the canthi and the alae nasi always remain free of lesions.

The eruption is roughly symmetric and mildly pruritic or asymptomatic and consists of firm superficial slightly elevated nonhyperemic papules, varying in size in the same patient from that of a pinpoint to that of a pinhead and rarely to that of a match head. The initial lesion is almost always partially depigmented to a varying degree, but on occasion it may be flesh colored or even deeply pigmented. Mildly hyperkeratotic lesions have also been noted. Inflammatory areolas are lacking, and hyperpigmented ones are also absent, except in the case of a deeply pigmented papule. This tuberculid has a tendency to appear in small groups, but actual fusion of papules has not been encountered. Sometimes small irregular-shaped areas of partial depigmentation may develop years before or subsequent to the appearance of the papular element, but there is always a gradual restoration to normal color regardless of treatment. This disturbance of pigment formation may be seen anywhere on the body, but it is most commonly observed on the face.

The eruption resolves spontaneously after a variable period, usually within several weeks, but it has a tendency to relapse. After complete healing, minute areas of depigmentation are frequently noted, but resolution of an occasional papule is sometimes followed by a slightly depressed

From the Department of Dermatology and Syphilology of the Harlem Hospital, Dr. Oswald La Rotonda, Medical Director



depigmented less often by hyperpigmented—atrophic scar corresponding in size to the original lesion

The superficial lymph nodes often show slight to moderate enlargement. They are discrete, freely movable and painless, and the overlying skin is normal. Symmetric involvement of the posterior cervical lymphatic chain is common. In my cases roentgenograms of the chest disclosed rather frequent enlargement of the mediastinal lymph nodes, but pulmonary tuberculosis was not encountered.

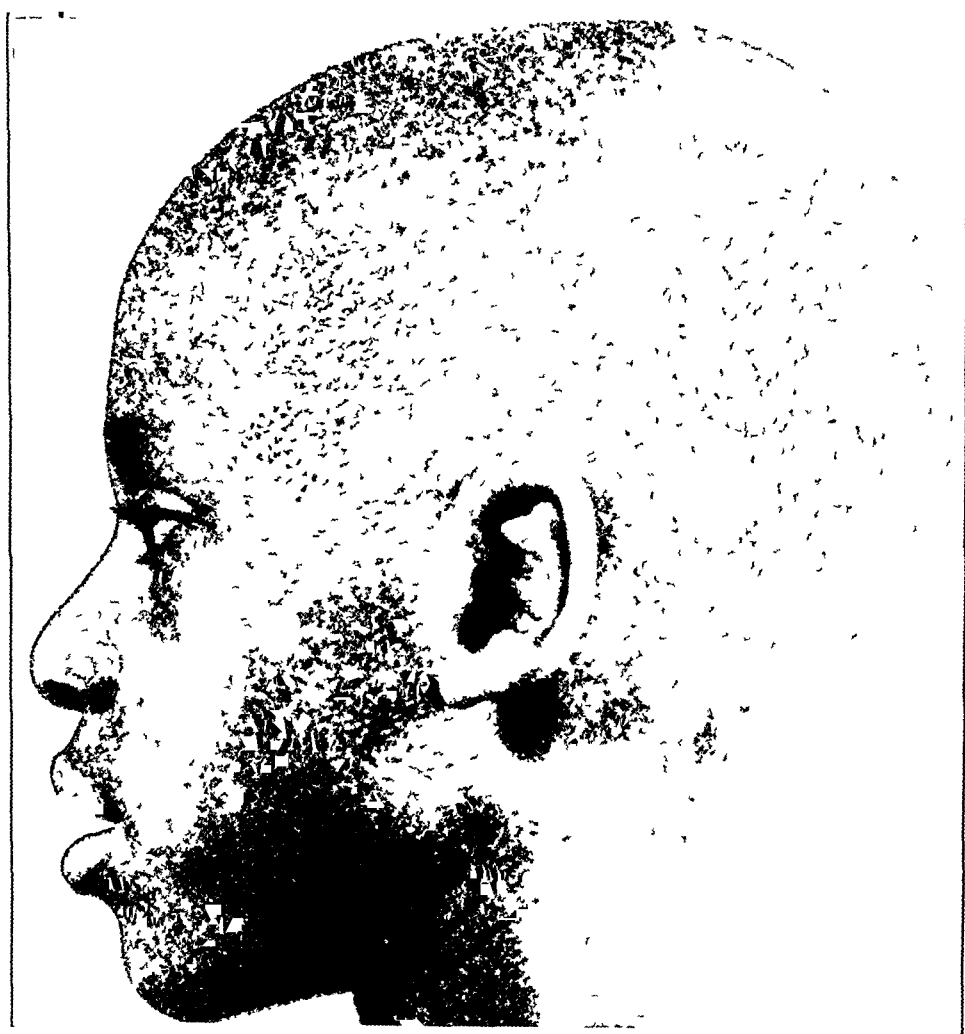


Fig 1—An unusually profuse eruption of micropapular tuberculid with involvement of the scalp

The ages of the patients ranged from 4 to 43 years, and females were affected most often. On the patient's admission the eruption had been present from several weeks to five years. The majority were asymptomatic, although anorexia, lassitude and loss of weight were not uncommon complaints.

The results of the tuberculin tests fluctuated considerably, some showed a negative local response to an intracutaneous injection of 0.1 cc

of old tuberculin in a dilution of 1 : 500, while others reacted strongly to a dilution of 1 : 100,000. Hemograms often showed mild secondary anemia with lymphocytosis and monocytosis.

*Histologic Study*—The epidermis directly above that part of the cutis showing the most intense reaction was likewise the most severely affected. For the most part it was atrophic, but it varied from normal thickness



Fig. 2—Resolution of papules followed by partial depigmentation

to slight hypertrophy. The stratum corneum was slightly thickened as a rule and at times was replaced by parakeratosis. The granular layer was noticeably irregular but was most commonly represented by a single row of cells, some of which were mildly edematous. The prickle cell layer was usually narrowed, but proliferative tendencies were observed at rare intervals both in the suprapapillary rete and in the rete

pegs Mild intercellular edema was a concomitant feature, and intracellular edema progressing to vacuolar degeneration appeared to be a constant observation In 1 case destruction of the more superficial prickles resulted in multiple vesicle formation The basal cells showed similar edematous and degenerative changes The amount of melanin in the basal layer was reduced noticeably or absent within small segments of the same section Complete loss of pigment was anticipated whenever severe edematous reactions developed in the basal cells and the neighboring prickles, and here the epidermis was invaded by such



Fig 3—Irrregular areas of primary facial depigmentation which preceded the development of papules

large numbers of small lymphocytes that the line of demarcation between epidermis and cutis was almost obliterated A number of moderately dilated hair follicles were filled with keratin, and their walls were either normal or showed changes similar to, though less severe than, the aforementioned epidermal alterations

Abnormalities occurred in all parts of the cutis but were detected most often in the upper half and still more frequently in the upper fourth of this layer, the subpapillary and adjacent underlying tissues being

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affected particularly. Well defined and compact perivascular and perifollicular collections of infiltrating cells differed in size but were usually



Fig 4—Micropapular tuberculid in an adult, showing generalized distribution

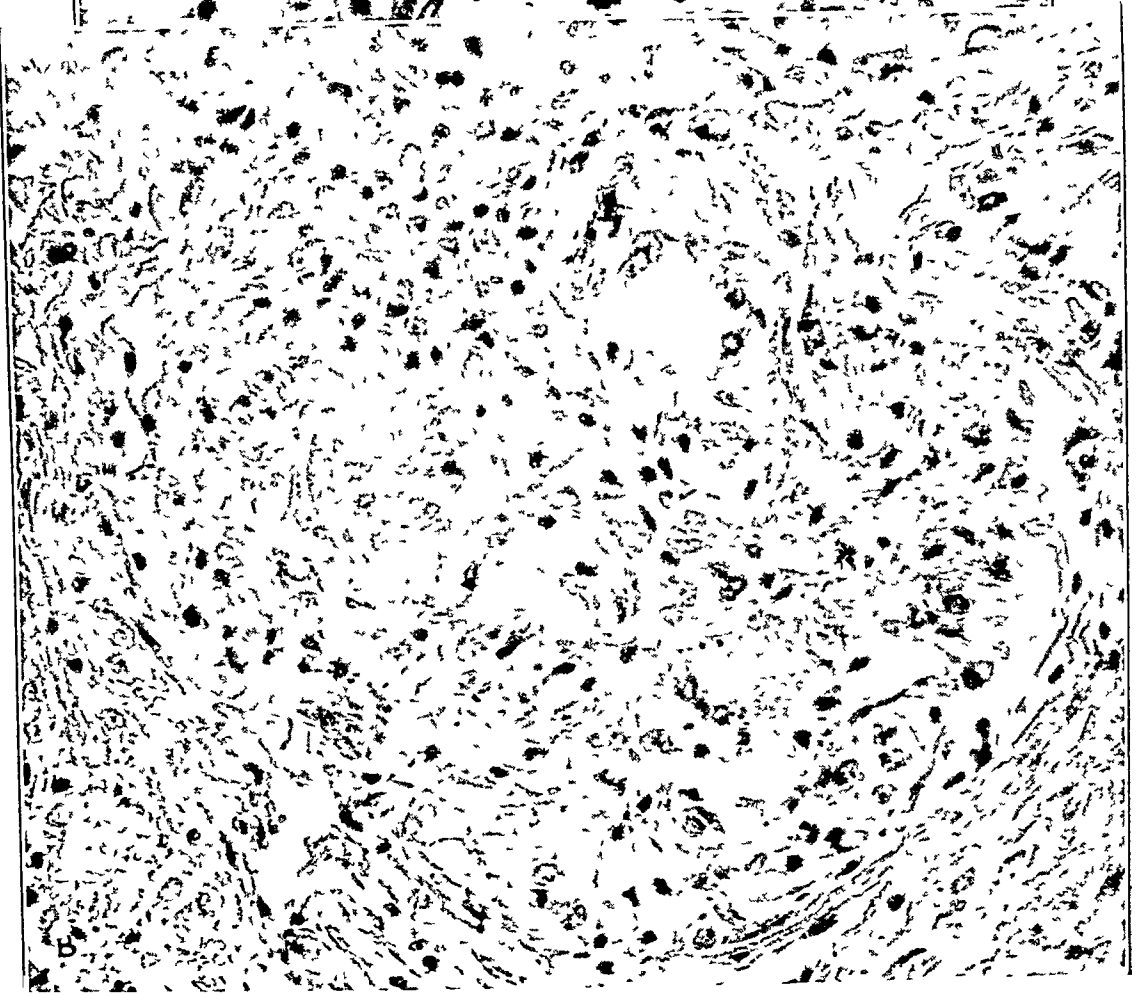
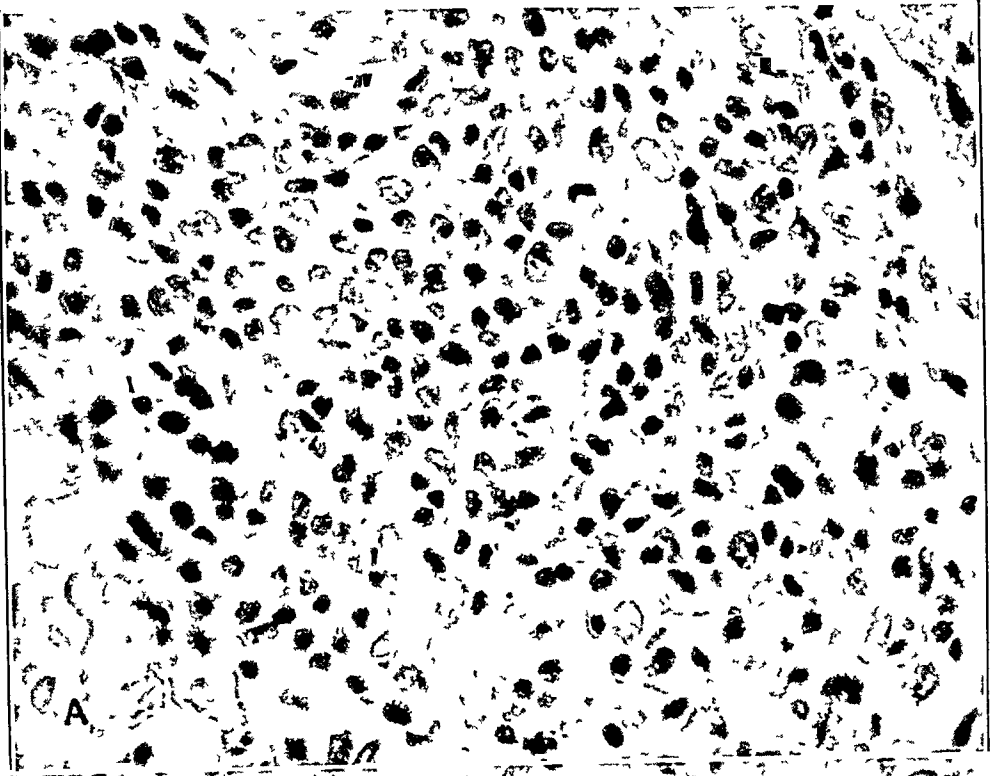
small and consisted chiefly of small lymphocytes, with diverse numbers of epithelioid cells and few plasma cells. The character of the infiltrate

varied from a purely banal type to that of typical tubercu'oid structure, either with or without tubercle formation. Lymphocytic nodules containing a scattering of minute groups of epithelioid cells were observed most commonly. Fibroblastic reactions about and within the infiltrate varied with the degree of healing. The supportive tissues were edematous and occasionally underwent granular degeneration, but necrosis was never observed. The superficial blood vessels were expanded somewhat,



Fig 5—The inflammation is most often limited to the superficial parts of the skin. The perivascular cellular infiltrates are well defined and compact. The epidermis is irregular, varying from atrophy to slight hypertrophy. (Low power magnification, hematoxylin and eosin.)

within some, the lining endothelial cells were swollen, and some showed decided proliferative tendencies. Pressure of the enveloping infiltrate often obliterated their lumens, and injury to their walls resulted frequently in thrombus formation and infrequently in milary hemorrhages. The superficial lymphatics were also dilated, and this reaction was



(See legend on opposite page)

evident particularly in the perivascular channels. In the superficial parts of the cutis both light and heavy deposits of melanin were found lying both free and within phagocytic cells.

Within the subcutis abnormalities were observed rarely and were of limited extent, but any part of this layer was subject to pathologic change. The infiltrate was well defined and consisted for the most part of small lymphocytes with a scattering and/or minute aggregations of epithelioid cells, together with an occasional giant cell. However, unlike the corium, typical tuberculoid structure and degenerative changes within the connective tissues were not encountered.

#### COMMENT

Micropapular tuberculid in a Negro has a distinctive clinical appearance. superficial firm discrete partially depigmented minute papules, lacking clinical hyperemia, persisting for relatively short periods and on healing leaving minute zones of depigmentation and less often slightly depressed depigmented atrophic scars. The lesions of micropapular tuberculid have not been noted on the canthi, the alae nasi or the vermilion border of the lips, the favorite sites for milium sarcoid and tuberculosis miliaris disseminata faciei.

Obviously in the presence of a banal type of inflammation the microscope offers no direct diagnostic assistance. In the presence of tuberculoid structure it is not possible to differentiate this disease from milium sarcoid and tuberculosis miliaris disseminata, the last-named disease is also included in this statement because it does not always show the classic tubercle.<sup>1</sup> It is quite evident, then, that the clinical features of micropapular tuberculid take precedence over microscopic observations. The tuberculin test is of no value in differential diagnosis because in some patients dilution as low as 1:500 may elicit negative reactions while in others there may be reactions to a dilution of 1:100,000. These conclusions are in accord entirely with those of Laymon and Michelson,<sup>2</sup> who have made a thorough study of this disease.

1 Ormsby, O. S., and Montgomery, H. *Diseases of the Skin*, ed. 6, Philadelphia, Lea & Febiger, 1943, p. 836.

2 Laymon, C. W., and Michelson, H. E. *The Micropapular Tuberculid*, *Arch. Dermat. & Syph.* **42**: 625 (Oct.) 1940.

#### EXPLANATION OF PLATE

Fig. 6—*A*, cellular infiltrate composed largely of small lymphocytes and epithelioid cells in varying proportions. As a rule, true tuberculoid structure is lacking. View of infiltrate shown in figure 5. *B*, view of infiltrate from another section showing typical tuberculoid structure. Note the similarity to the tubercle of milium sarcoid. (High power magnification, hematoxylin and eosin.)

Micropapular tuberculid differs clinically in Negro and in white patients. In Negroes the papules are nonhyperemic, depigmented and less often flesh colored or hyperpigmented, and there is a tendency toward generalization. Primary partial depigmentation does not occur in white patients. In the latter the papules are reddish or pinkish, suggesting rosacea, and generalization of the eruption has not been reported.

#### SUMMARY

In Negroes the lesions of micropapular tuberculid are usually sparse, but there is a tendency toward generalization.

The canthi, the alae nasi and the vermilion border of the lips are not involved in micropapular tuberculid, but they are the sites of predilection for milium sarcoid and tuberculosis miliaris disseminata faciei.

Partial cutaneous depigmentation may precede the papules for a variable period or develop subsequent to their appearance. Pigmentary disturbances are noted most commonly on the face.

Micropapular tuberculids usually leave depigmentation at sites of healing. Sometimes small, slightly depressed depigmented atrophic scars develop, and these sequelae are sometimes indistinguishable from those which follow the healing of superficial papulonecrotic tuberculids.

The tuberculin test is without value in differential diagnosis.

The microscopic picture varies from that of a banal type of inflammation to that of a typical tuberculoid structure. In the presence of the latter there is a remarkable resemblance to milium sarcoid and tuberculosis miliaris disseminata.

From a diagnostic standpoint the clinical characteristics of micropapular tuberculid take precedence over the microscopic.

In Negro patients the clinical characteristics of micropapular tuberculid vary considerably from those in white patients.



# Clinical Notes

## DDT IN THE TREATMENT OF SCABIES, LARVA MIGRANS AND PEDICULOSIS PUBIS

ANDREW G. FRANKS, M.D., LL.B., NEW YORK, AND WILLIAM L. DOBES, M.D., ATLANTA, GA

A clean, rapid and nonirritating treatment for scabies and pediculosis pubis, consisting of application of benzyl benzoate, has frequently been reported on. It is our purpose to report on a method of using and the effectiveness of DDT (dichlorodiphenyltrichloroethane) with or without benzyl benzoate in the treatment of scabies, larva migrans and pediculosis pubis. A formula containing the two active ingredients was recommended by the United States Department of Agriculture, Bureau of Entomology and Plant Quarantine. One of the modified formulas which we employed was as follows:

	Gm. or Cc
Benzyl benzoate	68
DDT	6
Ethyl aminobenzoate	12
Aerosol (diethyl sodium sulfosuccinate)	14

This concentrate is diluted with 5 parts of water. Eight patients with scabies were treated with the emulsion containing the DDT and benzyl benzoate. The medicament was applied over the entire body, except the scalp and face, with the hand, gauze or a 2 inch (5 cm) varnish brush. One application was employed in 7 cases. In 1 case a second application was needed. The emulsified formula has some distinct advantages. It has no disagreeable odor, it is easy to apply and does not soil the bed linen or the clothing. Only a thin residue is left on the body, which can easily be removed by soap and water. No frank case of dermatitis was noted, although the formula was irritating when applied to the excoriated surface, the irritation was not severe. On the unbroken skin no irritation resulted. The inclusion of ethyl aminobenzoate in the formula aids as a local anesthetic in relieving the itching, which may be severe in scabies.

Four patients with scabies were treated with the same ingredients without benzyl benzoate in a vanishing cream base. No patients responded favorably after one or more applications.

Four patients with generalized scabies were treated with DDT (10 per cent) in purified talc. The affected parts were well covered with the powder. Liberal amounts were dusted between the sheets. Scabies persisted in all 4 cases. No beneficial response was obtained.

The same formulas, the emulsion and cream preparations, were also employed in the treatment of pediculosis pubis in 9 cases. Again, one application of the medicament was sufficient for a complete cure. DDT (10 per cent) in purified talc was employed in 2 cases of pediculosis pubis. A total of 120 Gm was sufficient to check the infestation in both cases. Four patients with larva migrans were also treated with DDT in a cholesterol ester-petrolatum base (Aquaphor). No one responded to this treatment.

In brief, our cases show that DDT without benzyl benzoate was ineffective in the treatment of scabies and creeping eruption. DDT in combination with benzyl benzoate was found most effective against scabies. Yet this formula has practically no advantage over the usual benzyl benzoate emulsion. DDT in emulsion, ointment and powder formulas was found exceedingly effective in the treatment of pediculosis pubis. No harmful reactions occurred when DDT was used cautiously and in the therapeutic dosage in these cases.

# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

CUTANEOUS MANIFESTATIONS OF FUNGI ROYAL M MONTGOMERY and ESTHER A CASPER, J A M A 128 77 (May 12) 1945

In New York, the majority of cases of dermatophytosis are caused by *Trichophyton gypseum*, with *Trichophyton purpureum*, *Monilia albicans* and *Epidermophyton inguinale* causing the others. *T. gypseum* produces an acute inflammatory type of dermatophytosis in which vesiculation is the main feature. Infection of the nail plate is usually superficial and is manifested by scaling or small irregular white areas. *T. purpureum* evokes a noninflammatory dermatophytosis characterized by fine branny scaling and an absence of vesiculation. In infections of the nails this fungus invades the under portion of the nail, causing yellow undermined areas. Infections of the feet with *M. albicans* are characterized by red and macerated areas usually involving all the interdigital webs. Associated paronychia is a characteristic feature when infection of a nail occurs. The lateral borders of the nail plate are ridged and undermined. In infection of the feet with *E. inguinale*, maceration and severe scaling on the interdigital webs and flaky scales on the sole are observed. Frequently a concomitant infection of the groin is present. Onychial infection is absent. The basic principle of treatment for dermatophytosis of the feet is the use of soothing wet dressings or pastes in the vesicular stage and of fungicidal remedies after the acute phase has subsided. Strong fungicides must be used to treat *T. purpureum* infections. In onychomycosis all infected nail tissue should be removed before one applies fungicides.

BORIC ACID OINTMENT INTOXICATION CARL C PFEIFFER, LOIS F HALLMAN and ISADORE GERSH, J A M A 128 266 (May 26) 1945

Boric acid is absorbed in toxic quantities from ointments applied to burned areas or to wounds involving loss or damage to large areas of skin. It is absorbed also when it is used to irrigate cavities. Boric acid is accumulated in the brain, liver and body fat. Boric acid fails to appear in the urine when it is administered as a saturated solution or ointment to the torso of the normal human subject, absorption of boric acid through the intact skin is negligible.

PENICILLIN FOR NEUROSYPHILIS DOUGLAS GOLDMAN, J A M A 128 274 (May 26) 1945

Eighteen patients with dementia paralytica and 4 patients with tabes dorsalis were treated with penicillin. The patients with dementia paralytica were treated with a combination of intraspinal and intramuscular injections of penicillin or with fever and intramuscular injections of penicillin alone. Except for 2 moribund patients all patients with dementia paralytica were benefited. The patients suffering from tabes were given six daily intrathecal injections of penicillin. The total dose was 100,000 units. The 2 patients in this group who had tabetic crises were rapidly relieved. Observation of the other 2 ataxic patients was too brief to be conclusive, although it was noted that some improvement occurred.

NODULAR VASCULAR DISEASES HAMILTON MONTGOMERY, PAUL A O'LEARY and NELSON W BARKER, J A M A 128 335 (June 2) 1945

The term "nodular vasculitis" is applied to relatively chronic, persistent or recurrent nodular lesions of nontuberculous origin occurring chiefly on the legs, below the knees. Nodular vasculitis occurs in older women and has less tendency to become ulcerated than does erythema induratum. Histopathologically, there is a definite vasculitis with varying degrees of obliterative changes in both arteries

and veins together with necrosis of fat and fibrosis in the subcutaneous tissues. The authors would abandon the terms "periphelebitis" and "phlebitis nodularis necrotisans" because they have been used to represent both tuberculous and non-tuberculous conditions.

They employ the term "erythema induratum" to designate a tuberculous process - either of an ulcerative or of a nodose form. The disease usually is described as beginning with involvement of the calves of girls during adolescence, but it also may occur among boys and men and may start at any age in life. Seventy-two of the 175 cases on which this report is based are classified as cases of erythema induratum.

In both erythrocyanosis and pernio there are recurrent attacks which occur in the winter and disappear in the summer. The ulcers of pernio are usually more superficial than are the ulcers of erythema induratum, and the degree of inflammatory reaction is not as great in pernio as it is in erythema induratum.

Erythema nodosum is an acute process which undergoes involution without ulceration. The disease has often been associated with streptococcic infection. Like erythema induratum, relapsing, febrile, nodular, nonsuppurative panniculitis is frequently accompanied with attacks of fever. There are large subcutaneous plaques and cutaneous nodules, predominating on the trunk and thighs rather than on the legs, and the subsequent subcutaneous atrophy results in depression of the skin at the site of involution.

Primary recurrent idiopathic thrombophlebitis affects men rather than women. It is primarily a disease of small and medium-sized veins and is characterized by multiple discrete and tender nodules which tend to occur in crops and to extend by segments to the larger veins. Chronic venous stasis may produce a tender, painful plaque-like induration of the skin and subcutaneous tissues in the lower third of the leg. All these diseases are associated with varying degrees of vasculitis and fibrosis and with varying degrees of acute or chronic panniculitis.

**PENICILLIN SODIUM FOR FUSOSPIROCHETOSIS** WILLIAM F PEARCE and JOHN B McDONALD, *J A M A* **128** 342 (June 2) 1945

Fifty patients with fusospirochetosis were treated with intramuscular injections of penicillin sodium with doses of either 10,000 or 20,000 units every two or three hours night and day until a total of 100,000 to 200,000 units had been given. Complete alleviation of symptoms and eradication of the causative organisms were effected within twenty-four hours after the institution of therapy. Older methods of treatment required daily care and observation for a minimum of ten days and usually much longer. Treatment is reduced to three days by the administration of penicillin. Serologic studies at intervals are recommended to avoid masking of the development of early syphilis.

**NONFLUORESCENT RINGWORM OF THE SCALP** OSCAR L LEVIN and HOWARD T BEHRMAN, *J A M A* **128** 350 (June 2) 1945

Some fungous infections of the scalp do not impart a noticeable fluorescence to the diseased hairs. Examination under Wood's light with negative results is not sufficient to exclude these infections. Microscopic and cultural examinations are essential in suspected cases of ringworm of the scalp. Under Wood's light, hairs infected with *Trichophyton violaceum*, *Trichophyton sulfureum* and *Trichophyton crateriforme* show a dull white fluorescence which may be overlooked. *Trichophyton gypseum* and *Trichophyton purpureum* do not impart fluorescence to the diseased hairs.

**TREATMENT OF DEMENTIA PARALYTICA WITH PENICILLIN** CLARENCE A NEYMANN, GERT HEILBRUNN and G P YOUNG, *J A M A* **128** 433 (June 9) 1945

The hematoencephalic barrier cannot be overwhelmed by massive or long-continued intramuscular or intravenous doses of penicillin, it does not yield to combined treatment of either penicillin and bile salts or penicillin and artificial

fever The intracisternal route is dangerous if more than 30,000 Oxford units is injected Daily injection of this dose over a period of more than five days is also hazardous

Five patients suffering from chronic dementia paralytica were treated Two of them died from chronic encephalopathy attributable to the penicillin ten days after the last intracisternal injection Another patient died as the result of exhaustion two weeks after treatment ceased After intrathecal injections the serologic reaction changed in 2 of the cases, becoming practically negative One patient remains as demented as he was in the beginning, the other is decidedly improved

DERMATITIS OF THE LIDS FROM PENICILLIN ELIAS SELINGER, J A M A **128**:437 (June 9) 1945

Selinger reports a case of contact dermatitis of the eyelids after the instillation of a solution of penicillin into the conjunctival sacs of a patient treated for bilateral chronic conjunctivitis The conjunctivas and corneas showed no reaction A patch test with a solution of penicillin elicited a negative reaction

CERVICOFACIAL ACTINOMYCOSIS GLENN G HENDRICKSON and EDWIN P LEHMAN, J A M A **128** 438 (June 9) 1945

The authors report 2 cases of cervicofacial actinomycosis treated successfully by penicillin without the employment of surgical drainage They recommend that in all proved cases of actinomycosis intensive penicillin therapy without immediate surgical drainage be instituted If the organism is found insensitive to penicillin either by laboratory demonstration or by clinical response or by both, then and only then is the standard surgical attack justified

HENSCHEL, Denver

EVALUATION OF THE HISTAMINE INTRADERMAL TEST AS A GENERAL INDICATOR OF ALLERGY LAURENCE FARMER, J Allergy **16** 44 (Jan) 1945

The results of intracutaneous tests with 0.01 mg of histamine phosphate in 0.05 cc of isotonic solution of sodium chloride, administered to 77 persons with clinical allergy and to 9 nonallergic persons, led the author to conclude that "it is not possible to differentiate allergic individuals from nonallergic ones by the use of an intradermal histamine test"

SEASONAL DERMATITIS DUE TO THE ALBUMIN FRACTION OF TIMOTHY POLLEN JOHN H MITCHELL and WILLIAM F MITCHELL, J Allergy **16** 48 (Jan) 1945

The authors report a case of fairly generalized papular dermatitis in a 21 year old woman Attacks of dermatitis recurred for seven years during the pollination season of timothy grass (early June to the middle of July)

Patch tests with the oil of timothy pollen and plant elicited negative reactions, a patch test with the albumin fraction of timothy pollen elicited a strongly positive reaction, and a patch test with blades of timothy grass also gave a positive reaction

Scratch and intracutaneous tests with an aqueous extract of timothy grass in a dilution of 1:1,000 did not produce immediate wheal type reactions However, twenty-four hours later "there was an area of dermatitis extending several inches from the point of injection"

Ninety per cent improvement was accomplished by biweekly subcutaneous injections of an aqueous extract of timothy grass in small, increasing doses, the maximum tolerated dose was 0.3 cc of a 1:10,000 dilution Injections were given throughout 1943 and 1944

ALLERGIC DERMATITIS DUE TO METALLIC COBALT LOUIS SCHWARTZ, SAMUEL M PECK, KENNETH EDWIN BLAIR and KENNETH E MARKUSON, J Allergy **16** 51 (Jan) 1945

The authors report on 20 patients in whom dermatitis developed after they had worked for about one month in a plant that manufactures cemented carbides The

eruption was of the erythematous, papular type and lesions involved the cubital spaces, flexor portions of the forearms, backs of the hands and the eyelids. In a few patients the eruption was generalized.

Patch tests with metallic cobalt powder and a loose black powdery mixture containing all metals elicited positive reactions in 6 workers tested. The other ingredients of cemented carbides, including tungsten, tantalum, titanium carbides and carbon, gave negative reactions. The authors conclude that cobalt was the cause of the dermatitis.

Practical preventive measures are outlined.

MENDELSON, New York

**BONE LESIONS OF CONGENITAL SYPHILIS IN INFANTS AND ADOLESCENTS** P. E. Russo and L. F. SHRYOCK, *Radiology* **44** 477 (May) 1945

In 46 syphilitic children, the highest incidence of lesions of bone were found in infants less than 5 months of age, the predominant osseous lesions were generalized osteochondritis and periostitis. After the first year osteitis and osteomyelitis were the lesions most frequently found, usually associated with a periostitis.

**THE TREATMENT OF POST-IRRADIATIONAL ULCERS BY RADON OINTMENT** A. G. S. COOPER and D. F. ROBERTSON, *M. J. Australia* **1** 297 (March 24) 1945

Of sixty-nine malignant ulcers treated by radiation, twenty recurred, forty-one have been completely healed and eight have improved. The lesions were treated by radon-impregnated petrolatum as outlined by Uhlmann. Cooper and Robertson gained the impression that the alpha ray therapy in small dosage stimulated and promoted the growth of vascular epithelial tissue. The treatment does not add further damaging irradiation to an area already too heavily irradiated. Although beta and gamma rays are also emitted as a result of decay of radon in the ointment, they produce an ionization density no more than one hundredth that from the alpha rays to which the recovery of tissue is attributed. The ointment used does not have any retarding effect on a malignant lesion.

**THE INFLUENCE OF MALARIA ON THE KLINE AND COMPLEMENT FIXATION (WASSERMANN) TESTS FOR SYPHILIS** C. B. COX and M. J. DURANT, *M. J. Australia* **1** 320 (March 31) 1945

Seventeen doubtful and positive reactions to the Kline test were obtained in a total of 175 specimens of serum from nonsyphilitic patients suffering from acute malaria. In this series of specimens but four weak positive reactions to the Wassermann test were obtained. In 140 specimens of serum from nonsyphilitic patients convalescent from malaria 22 doubtful or positive reactions to the Kline test were obtained. In this series there were but three positive reactions to the Wassermann test.

Correspondence in serologic reactions was not seen with serum tested during both the acute and the convalescent stage. There is little risk of branding a patient with malaria as syphilitic if repeated examinations of the serum are made at intervals, both a flocculation test and a complement fixation test being employed.

HENSCHEL, Denver

**LYMPHADENOSIS BENIGNA CUTIS. CLINICAL AND PATHOLOGICAL STUDY** B. BAFVERSTEDT, *Acta dermat-venereol.*, 1943, supp. 2

An attempt is made to classify and clarify the confusing situation which exists with respect to a group of tumors of the cutis and subcutis which are composed of lymphoreticular tissue and characterized by a benign course.

In the past, two types of such tumors have been differentiated: (1) Spiegler-Fendt sarcoid and (2) lymphocytoma. Bafverstedt is of the opinion that the classification should be revised and that tumors described under these two headings constitute one entity. He suggests a new term for this widened conception, "lymphadenosis benigna cutis."

On the basis of this new classification, materials from 41 cases were studied, and a review was made in respect to clinical appearance, histology, etiology, pathogenesis, differential diagnosis, treatment and prognosis of this disease

Lymphadenosis benigna cutis attacks persons of all ages and occurs two to three times more frequently in women than in men. The tumors involving the cutis and adjoining parts of the subcutis are bluish red and vary in size from small nodules to tumors of the size of a closed fist and plaques several times as large as a man's palm. These lesions may disappear spontaneously, sometimes leaving atrophic scars.

Two forms of the disease can be distinguished: (1) isolated tumors which may appear in several localized regions and (2) multiple disseminated tumefactions. The former occur in persons of all ages and are most common on the face, lobes of the ears, nipples and scrotum. These are slow growing and seldom recur after treatment. The latter, which are comparatively rare, attack older persons and appear in several regions of the body simultaneously. The tumors in this form are large and deep and have a protracted course and a tendency to recur.

The tumors are made up of reticuloid and lymphocytic cells in a thin argentophile reticulum to form a lymphoreticular mass. The reticuloid cells usually predominate. The presence of plasma cells and swelling or proliferation of the fascicular endothelium are constant findings. This is the general picture of lymphatic tissue after slight or moderate inflammation. In these tumors, in addition, polymorphonuclear leukocytes are sometimes present.

The disease is definitely benign. There is no evidence of similar lesions in places other than the skin. There is no change in the normal blood picture. The only change in the hemopoietic system is a mild occasional regional lymphadenitis. Malignant degeneration has never been demonstrated.

The cause is unknown, but the author believes that in many instances the disease is a peculiar type of reaction to irritation, which may be pruritus, trauma, an insect bite and, possibly, venous stasis. It occurs occasionally in conjunction with atrophic or sclerosing processes (acrodermatitis atrophicans, scleroderma, cutaneous nodules, and others). The diagnosis, to be other than presumptive, must be made by histologic examination. Examination should include smears of blood and possibly of bone marrow.

The disease must be differentiated from leukemic or aleukemic lymphadenitis, Boeck's sarcoid, lupus erythematosus tumidus, round cell sarcoma and polymorphous sarcoma.

Both varieties are highly sensitive to irradiation. After roentgen ray therapy, the isolated tumors do not as a rule recur. The multiple disseminated type does recur, and no statement can be made as to whether a complete recovery is possible. For the latter type, arsenic has been administered with varying success.

The prognosis as to life is good in both varieties. As to recovery, it is good in the isolated form but doubtful in the multiple disseminated form.

THE SEDIMENTATION RATE IN SYPHILIS T STRYJECKI, *Acta dermat-venereol*  
21 605 (Aug) 1940

Although the increase in the sedimentation rate is not specific or characteristic for any disease and only points to a disturbance in the protein system of the plasma, the author feels that it is of value in the diagnosis and prognosis of syphilis.

In primary lesions which on dark field examination are negative for spirochetes the increase in sedimentation rate (10 to 20 to 30 mm) will serve to differentiate the ulceration of syphilitic origin from one of nonsyphilitic origin. In the latter the sedimentation rate will be normal (3 to 5 mm). In a generalized syphilitic eruption the sedimentation rate will be accelerated (50 to 70 to 115 mm), while an eruption of nonsyphilitic origin will not reveal this acceleration. This phenomenon, therefore, permits one to make a differential diagnosis within an hour.

The Biernacki reaction also serves to differentiate cases in which positive serologic reactions are found in spite of maximum therapy (serologic fastness) from

those which show positive reactions with no or inadequate treatment (late latent syphilis) In the former the sedimentation rate would be 3 to 4 mm, while in the latter the rate would be accelerated In this respect it also aids in controlling the efficiency of antisyphilitic therapy, the sedimentation rate gradually being decelerated with effective therapy

CUTIS RHOMBOIDALIS NUCHAE F KOGOJ, *Acta dermat-venereol* **21** 631 (Aug) 1940

In a survey of 860 peasants in the mountainous country near Travnik in Yugoslavia, 22.79 per cent had cutis rhomboidalis nuchae, of which 72.72 per cent were over 80 years of age No cases of its occurrence were observed in persons under 23 years of age The principal provoking factor is the repeated exposure to ultraviolet rays at an altitude of 800 to 1,600 meters, with the possibility of tar acting as a sensitizing agent The disease was almost always bilateral, in only 1 case in 196 was it unilateral Colloid degeneration of the conjunctiva was constantly observed as an associated change In fact, a diagnosis of cutis rhomboidalis nuchae cannot be made unless the conjunctival degeneration is present Histologically, there are degeneration of both collagen and elastin and dilatation of the blood vessels Cutis rhomboidalis nuchae is, in Kogoj's opinion, not a precancerosis, such as farmer's or sailor's skin, but a degenerative atrophy

THE TREATMENT OF VITILIGO WITH INTRADERMAL ADMINISTRATION OF GOLD K L. YONG, *Acta dermat-venereol* **21** 657 (Nov) 1940

Nine patients with vitiligo and 1 with albinism were treated by injections of a gold compound (Iopion) The 9 with vitiligo were treated by the intradermal method, and the albino was treated by both intravenous and intradermal methods Ultraviolet ray therapy was given to 2 patients and then discontinued when the author decided that it was superfluous Pigmentation appeared at the site of injection in all the patients with vitiligo, irrespective of subsequent ultraviolet irradiation The treatment of the albinism was a complete failure, disproving, according to the author, that pigmentation is due to the local deposit of gold in the injected areas No serious side reaction developed in any of these patients, although a mild scaly dermatitis, which disappeared in one week when treatment was discontinued, appeared at the sites of injection in several patients

The author concludes that gold somehow stimulates the exhausted melanoblasts in vitiliginous areas and could not possibly help albinos, since in them melanoblasts are totally absent

CONGENITAL ECTODERMAL DYSPLASIA OF THE ANHIDROTIC TYPE O KOALUND-JORGENSEN and J F CHRISTENSEN, *Acta dermat-venereol* **22** 1 (Feb) 1941

Congenital ectodermal dysplasia of the anhidrotic type is characterized by the absence of sweat glands, deficient dentition, poor development of the scalp hair, saddle-shaped nose, atrophic rhinitis, and occasionally the absence of sebaceous and mammary glands

A review of the literature produced 58 cases, to which the authors add 2 of their own The patients in the 2 cases described were brothers, children of a consanguineous marriage

Sections of normal skins were examined microscopically and showed the absence of sweat glands, sebaceous glands and hair follicles

These patients suffered great discomfort due to the absence of sweat glands, with resulting lack of heat regulation In hot weather or on exertion, the body temperature became elevated and they suffered from headache and became dyspneic Any febrile infection made them acutely ill

In most of the authenticated cases in the literature the disease is familial In all but 7 cases the patients were males, and it is suggested that, like hemophilia, the dysplasia is inherited as a sex-linked recessive ROBINSON, Washington, D C



# Society Transactions

## PHILADELPHIA DERMATOLOGICAL SOCIETY

Carmen C Thomas, M D , *Chairman*

Reuben Friedman, M D , *Secretary*

Oct 20, 1944

### **Tinea Capitis, Partly Cured Twice with Local Applications, and Now Resistant to Treatment** Presented by DR JOHN F WILSON

W P , a white boy aged 3½ years, presented a patchy loss of hair two months ago He has been treated with 5 per cent iodine crystals in a wetting agent base On two occasions examination of the scalp under Wood's filter revealed no fluorescence It reveals, now, however, fluorescent hair The hair at present is shaved off

### **Tinea Capitis, Cured with Local Applications.** Presented by DR JOHN F. WILSON

C D , a Negro boy aged 8 years, presented a patchy loss of hair over the entire scalp about two months ago Examination with Wood's filter showed many fluorescent areas typical of ringworm of the scalp, and a culture of the hairs was reported positive for *Microsporon audouinii* The patient was treated with 5 per cent solution of iodine crystals in a wetting agent base for two months He now has a normal regrowth of hair, and examination under Wood's filter reveals no fluorescence

### **Tinea Capitis, Cured with Local Applications** Presented by DR JOHN F WILSON

M D , a Negro boy aged 11 years, presented a patchy loss of hair from the scalp a month ago Examination under Wood's filter showed fluorescent hairs A culture of the hairs produced no growth Culture of the hair from his brother had revealed *M audouinii* The patient was treated with local applications of 3 per cent chrysarobin, 5 per cent salicylic acid and 5 per cent ammoniated mercury in a wetting agent base for one month There is now a normal regrowth of hair, not fluorescing under examination with Wood's filter

#### DISCUSSION OF THE CASES OF TINEA CAPITIS

DR J V KLAUDER I think that Dr Wilson should enlarge on the fact that the disease in each case was cured and then recurred

DR JOHN F WILSON The question in the first case has been as to whether any of the hairs did fluoresce When first examined, the patient had fluorescent hairs throughout the entire scalp Then, after treatment for about a month, there was no more fluorescence At the end of another month or six weeks there was fluorescence again I cannot say whether that was due to the growth of still infected hairs beyond the level of the scalp or to reinfection I treated the patient again for approximately another month, and the fluorescence disappeared A month later, fluorescence reappeared Three months have since elapsed, and I have not been able to make the fluorescence disappear Because of the fact that I keep the heads of the patients closely shaven, it is difficult to remove any hair easily with

forceps and I have not attempted any more cultures. I feel that to the practiced eye there is no question whatever about what is fluorescence and what is not.

DR SIGMUND S GREENBAUM. Dr Wilson, I think, has accepted the conclusion, with which I agree, that Wood's filter is of no avail when the hair is below the level of the surface of the scalp. Cultures then are certainly indicated, if materials for culture are obtainable. In the white child the hair has grown fast enough to show that Dr Wilson's wetting agent has not effected a complete cure.

DR J V KLAUDER. Examinations under Wood's filter that repeatedly reveal no evidence of fluorescence overcome that objection. I do not think that any one regards a single examination under Wood's filter revealing no fluorescence as evidence of cure. In Dr Wilson's cases there were repeated examinations.

DR SIGMUND S GREENBAUM. Dr Wilson states that the Negro children have been observed for three or four months. I think that Negro children should be observed for longer periods than that because their hair grows so slowly. I do not think that one should regard the 2 Negro children as cured until a period of six months has elapsed.

DR JOHN F WILSON. We are now in the midst of an epidemic of ringworm of the scalp. If epilation by roentgen rays is the therapeutic answer to this epidemic, then why not examine under Wood's filter every child under the age of 13 or 14, under public health auspices, and then have every patient with ringworm receive epilation therapy with roentgen rays?

DR HERMAN BEERMAN. The problem is how to get all the necessary x-ray machines, personnel, Wood's filters and physicians capable of interpreting what the Wood filter reveals.

DR FRED D WEIDMAN. It takes money properly to combat this epidemic, and public health authorities must reconcile themselves to this fact. This is a matter that concerns children and their education in Philadelphia, and I think that success in the treatment can be achieved only by the use of roentgen rays, and that means money. It is an imposition to try to wheedle dermatologists and radiologists to take on this work gratis. Physicians ought to do so no more than lawyers ought to give their services for nothing in public matters. Epidemics of ringworm are ancient history. The epidemic in Paris was so severe that schools for children with ringworm were created, and the same was true in Edinburgh. The epidemic in Paris was not overcome until Sabouraud made arrangements for the children to be treated with roentgen rays, whereupon the ringworm schools soon closed. Another thing that annoys me is the fact that not enough dermatologists are using roentgen rays for epilation. This must be corrected, or else the reputation of dermatology will suffer. Incidentally, Dr C Guy Lane told me that he standardizes his apparatus with a Victor meter preceding each epilation.

DR CARMEN C THOMAS. There seems to be a feeling among radiologists that the modern x-ray tubes are somewhat dangerous to use because of too great concentration of the rays.

DR REUBEN FRIEDMAN. Our department of radiology refuses to give treatment in such cases. Its objection is based on a wholesome regard for the pituitary gland. It contends that it is not without danger to that gland to subject these youngsters to the cross-firing technic of roentgen ray epilation.

COMMANDER H E TWINING (MC), USNR. In a service of fifteen years at a local hospital there was no epidemic but there were many cases of tinea capitis. Thallium acetate was used for children under 12 years of age, strict attention being given to their weight and to the dosage. I never had any toxic effects in patients so treated. Why cannot thallium acetate now be used for children under 11 or 12?

DR REUBEN FRIEDMAN. In the last twelve or thirteen years I must have treated a minimum of 50 patients with thallium acetate (Merck). My results were uniformly good, although a considerable number of the patients had temporary mild toxic effects, chiefly in the form of neuritic pains in the lower extremities.

Last year I had occasion to treat 2 private and 2 clinic patients with thallium acetate, with unfortunate immediate sequelae, although all 4 ultimately made good recoveries. I have decided not to use the drug again.

DR JOHN F WILSON There is some question whether the domestic thallium acetate is pure enough. I have enough of the prewar drug to treat about 70 patients, and I have been considering using it. Incidentally, with tinea capitis so tremendously prevalent, what is to prevent recurrence after treatment? I have not felt that I wanted to use roentgen rays on patients and then send them out to take chances on reinfection.

DR SIGMUND S GREENBAUM I think that ringworm of the scalp in Negro children in Philadelphia is endemic and that it has become epidemic in the white children. I think that they get it from the back rests of the chairs in the motion picture houses. My experience with thallium acetate has been good over many years. In one case there was peripheral neuritis and in another muscular weakness, but the patients recovered. I am afraid of the drug and select the children to receive it.

DR BERNARD L KAHN About six years ago I treated 18 patients at a local hospital with thallium acetate. I had no trouble so long as the dosage was correctly measured, and I had the best results in children 6 to 12 years of age. One youngster in whom neuritis developed was found to be 13, whereas he had been entered as being 11 years old. He made a good recovery.

DR THOMAS BUTTERWORTH, Reading, Pa. I am not convinced that tinea capitis caused by *M. audouinii* cannot be cured by chemical means. There have been outbreaks at an institution for feeble-minded persons. They occurred at intervals in various cottages during the ten years that I have been connected with the institution. One of the most important requirements for successful treatment is attention to details and proper nursing care. The criterion for cure is to put the treated children back into a cottage with the other 75 or 80 children, and if an epidemic does not break out in a few months in that cottage it is known that the original patients were cured. In the program followed in this institution, the hair of the scalp is shaved weekly.

After the article on the use of diethylstilbestrol appeared, I prescribed 3 mg of the drug to be taken three times a day. I also used a preparation containing 6 to 12 per cent iodine crystals in equal parts of phenol and camphor. This was rubbed thoroughly into the scalps of the patients once or twice a day until it was felt that the children were cured. They were then sent back to their cottages, and there have been no epidemics in them. It is only recently that epidemic ringworm has reached Reading, although not to the degree now being experienced in the schools in Philadelphia. I think that the main thing in private practice is for the physician to tell the parents what he wants done, and if they do not do it to tell them to change physicians.

DR BERTRAM SHAFFER How much estrogenic substance do you administer?

DR THOMAS BUTTERWORTH, Reading, Pa. Three milligrams a day. If the breasts do not become enlarged and dark, there will not be any therapeutic effect. Some physicians use 5 mg.

DR J V KLAUDER I obtained a therapeutic effect with the use of 0.25 mg twice a day for three weeks. I was under the impression that I obtained an appreciable percentage of cures. However, when results in all the cases were tabulated, to my surprise it was found that only 2 out of about 30 patients were cured. Both were males.

DR SIGMUND S GREENBAUM I do not believe that an estrogenic substance will cure an infection of the scalp due to *M. audouinii*. It will rapidly cure children infected with animal ringworm. Three boys who contracted the infection from a dog were cured within a month after the administration of diethylstilbestrol. Later,

I used it for patients who appeared clinically to have *M. audouinii* infections but failed to obtain any cures

DR THOMAS BUTTERWORTH, Reading, Pa. I at first used 0.5 mg twice a day but did not get good results. Gynecologists whom I consulted were not amazed at the use of 3 mg, which is the dose they give in the treatment of vaginitis.

DR JOHN F. WILSON. There is a difference of opinion about that drug. Some endocrinologists feel that one cannot give large doses of it for any length of time with safety. One man brought up the question whether the untoward results are immediate or not. They may be delayed. In view of the dispute as to the efficacy of diethylstilbestrol and its questionable safety, one wonders whether it should be used at all.

#### **Vitamin A Deficiency Producing Follicular Hyperkeratosis** Presented by DR MARJORY K. HARDY

R. D., a Negro girl aged 9 years, pale and undernourished, presents on the extensor surfaces of the arms and forearms and on the dorsa of the hands and fingers hyperpigmented and hyperkeratotic follicular black papules. They have intrafollicular horny plugs producing a nutmeg-grater-like appearance. There are similar lesions on the extensor and flexor surfaces of the legs and the lower part of the thighs. The palms are dry and thickened. The patient has had the usual childhood diseases. Her diet is inadequate, consisting of cereals, pancakes, grits and bread. It is deficient in fruits and vegetables. A complete blood count revealed hemoglobin, 68.3 per cent (10.5 Gm.), erythrocytes, 3,920,000, and leukocytes, 6,850, with 39 per cent polymorphonuclear leukocytes, 54 per cent lymphocytes, 3 per cent monocytes and 4 per cent eosinophils. The patient was given 50,000 U. S. P. units of vitamin A by mouth for six weeks, with appreciable improvement. She has received 100,000 units of vitamin A by injection for the past five weeks, with 60 per cent improvement.

#### DISCUSSION

DR SIGMUND S. GREENBAUM. The child is decidedly undernourished, and one would wonder why there is not a vitamin C and vitamin D deficiency in addition. She has been on a grits and bread diet, which might take care of the vitamin B requirements, but it is hard to account for the others.

DR MARJORY K. HARDY. I think that this girl's case fits into the group of cases, described two years ago by C. N. Frazier and others (*ARCH. DERMAT. & SYPH.* 48:1-14 [July] 1943), of a deficiency disease observed in Chinese children, of whom it was mentioned that the dermatosis worsened as the children neared puberty.

#### **Morphea, Improved by Bismuth Therapy** Presented by DR J. V. KLAUDER

M. R., a white woman aged 48 years, was first seen on Oct. 11, 1944, at which time she presented on the left side of the chest a bandlike area of scleroderma about 6 inches (15 cm.) long and 2 inches (5 cm.) wide, the surface of which was smooth and white and hard to the touch. Its duration was about four months. There was no history of injury preceding the appearance of the lesion. Examination of the rest of the cutaneous surface revealed no abnormalities. The patient received one injection of 1.5 cc. of bismuth subsalicylate intramuscularly. One week later there was an apparent improvement in the lesion, inasmuch as the surface was wrinkled and the hardness was less pronounced.

#### DISCUSSION

DR FRED D. WEIDMAN. Why did you use the bismuth compounds?

DR J. V. KLAUDER. At the last meeting of this Society, Dr. Stokes mentioned treatment of this disease with a bismuth compound, citing a French report. He

reported striking results obtained from the use of bismuth hydroxide. Definite improvement followed the first injection and has continued following the second injection.

NOTE—The induration had practically disappeared following six consecutive weekly injections of the bismuth compound.

### **Pustuloulcerative (Frambesiform) Syphilid**

NIEDELMAN and DR MORRIS MARKOWITZ

Presented by DR M L

E D, a Negro man aged 47, presents numerous crusted and ulcerated lesions with a foul odor on the scalp, face and neck. There are also a number of papular lesions on the face. A few scattered crusted lesions are present on the body. The patient was circumcised about one year ago, at which time the serologic reaction of the blood was negative for syphilis. About five months ago, there developed a painless penile lesion which remained for one month. Following this, an ulcerative lesion appeared on the left palm followed by numerous papular lesions on the body and the face. The Kolmer-Wassermann reaction of the blood was strongly positive. The patient has had one intramuscular injection of a bismuth compound. I saw him for the first time three days ago.

NOTE—After four intravenous injections of oxophenarsine hydrochloride within a period of two weeks, the patient's lesions have almost disappeared.

### **DISCUSSION**

DR BERTRAM SHAFFER

A biopsy and culture should be performed to eliminate blastomycosis.

DR SIGMUND S GREENBAUM. It is most unusual for an early secondary syphilid to be ulcerative. It does ulcerate in precocious malignant syphilis. This looks more like a frambesiform type of syphilis.

### **Scleroderma, Generalized Progressive**

Presented by DR CARROLL S WRIGHT

R C, a white woman aged 35, early in 1942 noted thickening of her skin and difficulty in movement. During a pregnancy she improved temporarily, but otherwise the disease has progressed rapidly. There is a widespread typical scleroderma particularly involving the arm. The left elbow shows a superficial ulcer about 1 cm in diameter. The patient had been given diethylstilbestrol previously and has also received injections of estrogenic substances, a bismuth compound intramuscularly and massive doses of vitamin A intramuscularly, with no striking results. The patient is presented for therapeutic suggestions.

### **DISCUSSION**

DR SIGMUND S GREENBAUM. This is the type of case that the Mayo group, particularly O'Leary, have been describing for some years, in which the phenomena are closely associated with Raynaud's syndrome. In these cases O'Leary thinks that he has obtained good results with neostigmine.

DR CARMEN C THOMAS. I have found neostigmine more effective against the morpheaform type, in fact, any treatment is more effective against that type.

### **Sarcoidosis, with Involvement of the Nose**

Presented by DR MARJORY K

HARDY

This patient was presented before the Society in May 1942 (ARCH DERMAT & SYPH 47 444 [March] 1943).

C W, a Negro woman aged 38, thin and appearing younger than her given age, when first seen, in 1942, presented small soft papules around both eyes, a few lesions on the lobes of the ears and larger lesions on the lip. There was a non-painful swelling involving the lower part of the nasal septum. The lesions on the

lids and the ears have cleared, but the nasal lesions have increased in size, involving both sides of the nose. These lesions are hard and dusky red.

The report on a roentgenogram of the chest made in September 1944 was as follows. There were increased markings of the base of the right lung. Otherwise, the lungs were clear. There were nodular swellings at the end of the nose but no destruction of the nasal bone. A complete blood count revealed hemoglobin, 71.5 per cent (11 Gm.), erythrocytes, 4,210,000, and leukocytes, 5,350, with 42 per cent polymorphonuclear leukocytes, 36 per cent lymphocytes, 18 per cent monocytes, 2 per cent eosinophils and 2 per cent basophils.

In May 1942, Dr. Fred D. Weidman diagnosed the disease as tuberculosis from a biopsy specimen.

The cutaneous lesions have practically disappeared, except one on the upper lip. The nasal lesion has undergone about 25 per cent involution since the administration of gold sodium thiosulfate to a total of 400 mg.

#### DISCUSSION

DR. CARMLIN C. THOMAS: The local treatment of these lesions with solid carbon dioxide has given excellent results in a similar kind of tuberculosis with sarcoid-like features. There was rapid improvement.

DR. MARJORY K. HARDY: Two years ago there was involvement of one finger. There is no involvement of the nasal bone now. The original lesion selected for biopsy was a soft papular area on the back of the neck.

#### **Alopecia Cicatrisata** Presented by DR. J. V. KLAUDER

F. B., a white boy aged 16, has always, according to his mother, had bald areas on the scalp and sparse hair. Almost the entire top of the scalp is devoid of hair, and the skin is shining and atrophic. At the periphery of the bald area the hair is sparse and coarse and feels like straw. There are scattered pustules and red puncta which center around a hair follicle. The hair of the eyebrows and pubic region is scanty, and in some areas there is folliculitis. There are no hairs on the lids and chest or in the axillae.

The breasts are absent, as is the right nipple, the left nipple being rudimentary. The upper teeth are absent, the lower ones are poorly spaced and dwarfed. The skin is dry and coarse. There are lesions of keratosis pilaris on the thighs and forearms. The nails are unaffected.

The boy is apparently of normal intelligence. The parents are not related. He has three older sisters, who are in good health. His basal metabolic rate is -11 per cent. His mother said that when he was 9 years of age he was treated with a variety of glandular products, without apparent benefit.

The patient was first seen by me in June 1944. For a limited period a 5 per cent sulfathiazole ointment was used on the areas of folliculitis, subsequently a 6 per cent ammoniated mercury ointment was administered. It is still being used. In addition, he is taking 25,000 U. S. P. units twice daily of vitamin A and 2 teaspoons, three times daily of hydrolyzed wool (Brown, H., and Klauder, J. V. *Sulphur Content of Hair and of Nails in Abnormal States. Therapeutic Value of Hydrolyzed Wool, I. Hair*, *ARCH. DERMAT. & SYPH.* **27**: 584 [April 1] 1933) for its effect on sulfur metabolism. There has been no increase in growth of hair, but the folliculitis is less apparent and the general health of the patient has improved. He has gained weight. The skin is less dry, and the keratosis pilaris has improved.

#### DISCUSSION

DR. J. V. KLAUDER: I think that there has been an improvement in the patient's general health and in the decrease of the lesions of folliculitis following the therapy detailed in the protocol. I should like to study the sulfur balance. It would be interesting to see whether the balance is altered. The disease looks like a dystrophy of the keratin-forming apparatus, and that would be a pertinent study.

DR SIGMUND S GREENBAUM I think that a condition as diffuse as this is involves a dystrophy. The papillae of the tongue are absent, and I wonder whether there is any ectodermal defect in addition.

DR J V KLAUDER That brings up the question of how much these are related to the dystrophy.

DR BERNARD L KAHN Why did you give him hydrous wool fat?

DR J V KLAUDER Not hydrous wool fat, hydrolyzed wool. Hydrolyzed wool is a means of giving the sulfur protein compounds by mouth. There is no soluble form of organic sulfur. Sodium thiosulfate is one of the inorganic sulfur compounds, hence, Brown conceived the idea of hydrolyzed wool, which contains all the amino acid-containing sulfur compounds present in hair, notably cystine. The reason was to support the sulfur metabolism by giving these sulfur compounds.

DR FRED D WEIDMAN I have not followed this patient over weeks and months as Dr Klauder has, and I should like to ask him whether he feels that this patient appears to be older than his age. Since there is dystrophy of his teeth and a certain tendency to alopecia on his forearms, and so forth, maybe this is a case of sub-clinical progeria, premature senility. It seemed to me that this boy appeared to be older than 16 years.

DR REUBEN FRIEDMAN The semblance of senility is one of the symptoms that are seen in hereditary ectodermal dysplasia of the anhidrotic type. This case presents a double picture, one of folliculitis decalvans and the other of hereditary ectodermal dysplasia of the anhidrotic type.

DR FRED D WEIDMAN I thought of progeria, too, but the patient's nose is of the wrong type. He has a hooknose.

#### Chronic Lymphatic Leukemia, Cutaneous Lesions Following Irradiation Presented by DR JOHN W LENTZ

F R, a white woman aged 63, was admitted to the hospital on May 19, 1944 and discharged on June 9, with a diagnosis of chronic lymphatic leukemia. On this admission generalized lymphadenopathy and pronounced enlargement of the liver and spleen were noted. There is no record of any complaints relative to the skin. Physical examination disclosed no abnormalities of the skin. The patient returned to the hospital on September 11, with a chief complaint of successive crops of blebs that itched. They first appeared about August 20, on the arms and then developed on the face and finally on the abdomen, chest and back. There were none on the legs but some on the soles. Blebs appeared, opened and then dried. At this second admission, generalized lymphadenopathy was again noted. The skin was generally involved, with lesions on the chest, abdomen, back, and all four extremities. The lesions are small papules which develop into small bullae, 3 to 5 cm in diameter, containing clear fluid. A small area of inflammation was noted around each lesion. In addition, there were roughly circular areas, 1 cm in diameter, which were dark and hemorrhagic. The last were most pronounced on the forearms and ankles. The face was clear at the time of examination, although the patient states that papules have appeared there previously. There is severe pruritus.

A hemogram made in May 1944 revealed hemoglobin, 81 per cent, erythrocytes, 4,480,000, and leukocytes, 83,000, with 11 per cent neutrophils and 89 per cent lymphocytes. A hemogram in June, following roentgen ray therapy, showed hemoglobin, 68 per cent, erythrocytes, 3,850,000, and leukocytes, 7,700, with 64 per cent lymphocytes. The urine was normal, except for a faint trace of albumin on two occasions. The Wassermann and Kline reactions of the blood for syphilis were negative.

A roentgenogram of the chest showed no unhealed pulmonary disease but indentation and deflection of the trachea to the right, probably due to enlarged nodes.

Results of a urinalysis on the patient's second admission to the hospital proved normal

A hemogram made in September showed hemoglobin, 68 per cent, erythrocytes, 4,420,000, and leukocytes, 15,000, with 39 per cent neutrophils, 59 per cent lymphocytes and 2 per cent monocytes

Since May 1944, the patient has received roentgen ray therapy as follows. Divided doses to different fields were given at 200 kilovolts through a Thoreus filter. The totals to the various cutaneous areas are as follows: spleen, 828 r, right groin, 276 r, right axilla, 276 r, right side of neck, 254 r, left groin, 276 r, left axilla, 276 r, and left side of neck, 254 r.

The last treatment was given on August 4

#### DISCUSSION

DR JOHN W. LENTZ: One of the interesting things about this case is that the patient did not have any cutaneous lesions until after she had received irradiation.

DR FRED D. WEIDMAN: Before I saw the diagnosis recorded on the history sheet, I was struck with the rapidity of the development of these lesions, corresponding to the wheals which appear tonight. I wondered whether it was an unusual expression of woody edema. It would be remarkable for lesions of that size to develop as a result of proliferation of lymphocytes in leukemia. The tendency is to regard the lymphocytes as proliferating in situ in this disease instead of emigrating from blood vessels.

#### **Multiple Neurofibromatosis with Sarcoma (Now Excised)** Presented by DR CARMEN C. THOMAS

D. O., a white woman aged 23, presents over the trunk and extremities many various-sized brown macules, some pinhead sized, others 2 to 3 cm. in diameter. When the patient was first seen, in May 1944, a palm-sized brown irregular flat mass was present on the lower part of the left side of the thorax, with a lemon-sized ulcerating mass projecting from its surface. There are several soft skin-colored tumors, 1 cm. or more in diameter, present on the arms and thighs. These can be pushed below the cutaneous surface. Some of these tumors show telangiectatic surfaces. The patient has had a brown mole on the left side of her chest all her life. A hard lump developed there ten months ago and became ulcerated two weeks before admission to the hospital in May 1944. In 1937 she received three roentgen ray treatments to the left side of the chest. A nodule from the right side of the chest was excised on Oct. 22, 1940. A diagnosis of neurinoma was made.

A roentgenogram of the chest showed a cystic defect in the right tenth rib posteriorly. The skull and the left arm and right leg revealed no evidence of osseous involvement.

The report on the biopsy stated that the tumor consisted of bundles of spindle-shaped cells, some of which had elongated and had irregular nuclei. Occasional mitoses and multinucleated cells were seen. Numerous vessels were found in the mass, some of which contained tumor cells. The tumor was partly encapsulated. Its origin was probably in the perineural sheath. The diagnosis was perineural fibroblastoma (malignant von Recklinghausen's disease). The entire mass on the left side of the chest was excised and replaced with a full thickness skin graft on May 12, 1944. Since then the patient has gained weight and feels well.

#### DISCUSSION

DR CARMEN C. THOMAS: Have any of the members any views on the prognosis in this type of case after the removal of such a tumor?

DR BERNARD L. KAHN: I had a patient with involvement of the lower jaw. The result was fatal after about sixteen months.



**Arteriosclerotic Ulcer of the Leg** Presented by DR BERTRAM SHAFFER

S G, a white man aged 80, presents extensive but partially healed ulcerations involving the anterior and lateral aspects of the lower half of the right leg. Twenty years ago the patient fell and injured this leg. An ulceration developed, which persisted until the present time. Unna boots and various local applications in outpatient departments did not help. He was admitted to the hospital on Sept 11, 1944. He had "pus on his knee" twelve years ago. The veins on the right leg were "tied" ten years ago. He has a cataract in his right eye, a right inguinal hernia and generalized arteriosclerosis. The patient's Wassermann reaction was negative. The blood cell count and the blood chemistry were normal. He has shown striking improvement since the application of red blood cell paste of unknown composition.

## DISCUSSION

DR BERNARD L KAHN: I last saw this patient about four months ago. He had a pronounced purulent discharge on his right leg with a mixed infection, staphylococci predominating. Penicillin was injected, 20,000 units every four hours, but only enough was available for five injections. Within twenty-four hours the lesion practically dried, and the odor disappeared.

**Ulcers of the Leg (Trophic, Factitial, Arteriosclerotic, Traumatic?).**

Presented by DR BERTRAM SHAFFER

M M, a white woman aged 66, active and intelligent, presents a superficial ulceration on the outer aspect of each leg, near the ankle. The ulcer on the left leg is 10 cm in diameter and on the right is 5 cm in diameter. The granulations appear healthy and hypertrophic. Little reaction is found at the periphery of the lesions. They have a geometric outline. A "pimple" developed on the left leg eight months ago. One month later the right leg was injured. Both sites became ulcerated. She was admitted to the hospital on Sept 13, 1944. She has a hypertensive arteriosclerotic cardiovascular disease. The Wassermann reaction of the blood was negative. The blood sugar, blood urea nitrogen and urine were normal. The application of a red blood cell suspension of unknown composition produced a certain degree of improvement.

**A Case for Diagnosis (Arteriosclerotic Ulcer with Scleroderma-Like Changes, Ergotism?).** Presented by DR BERTRAM SHAFFER

L B, a white man aged 71, senile, not in good health, reveals that the skin about his ankles and feet, especially on the right side, is bound down, hard, sclerotic and pigmented. Pulsation of the dorsalis pedis arteries is not present. The dorsum of the right foot is the site of an indolent tender ulcer about 2 cm in diameter but originally about 8 cm wide. The great toe on the right foot was amputated thirty-five years ago. The middle toe on the left foot is atrophic, and the distal phalanx apparently is missing. An ulcer developed on the dorsum of the right foot three months before the patient's admission to the hospital on July 29, 1944. The only form of bread that the patient eats is rye bread. His diet otherwise is not remarkable.

The Wassermann reaction of the blood was negative. The blood sugar content was 70 mg and the blood urea nitrogen level 15 mg per hundred cubic centimeters. The blood count and urinalysis were within normal limits. The gastric acidity was normal. A roentgenogram of the foot revealed a localized area of osteitis on the bases of the third and fourth metatarsals of the right foot. The bones were otherwise atrophic. The neurologic examination disclosed no evidence of disease of the central nervous system. Peripheral vascular studies indicated that the ulceration was probably due to arteriosclerosis.

The patient has received exposures to ultraviolet radiation, ascorbic acid and nicotinic acid, 50 mg of each, have been given daily, and sulfathiazole, 0.8 per cent solution, has been used as a wet dressing. He was given a rye bread diet three days ago to see what effect it would have on the ulcer.

## DISCUSSION OF THE PRECEDING CASES

DR FRED D WEIDMAN The latter patient has been studied by the section on peripheral vascular disease of the hospital, which decided that the dermatosis was due to arteriosclerosis. The dorsum of the foot is hidebound and pigmented, morphologically the disease could pass for scleroderma. The ulcer, of course, goes with peripheral vascular sclerosis. This man gives a history of eating rye bread only when at home, and Dr Philip Custer some time ago told me personally that at one time he was in the habit of feeding scraps of rye bread from the table in his institution to his experimental rats and that gangrene developed in their tails and noses, which dropped off. Of course, all of us know about ergotism and the mold concerned in it, but it is doubtful that the mold in this case is connected with the rye bread eaten in Philadelphia. But it still remains that here is a man who does not eat white bread at home and has suffered necrosis of his toes.

DR SIGMUND S GREENBAUM These 2 patients were treated by me while on service during July, August and September. They are presented not because they have arteriosclerotic ulcers of the leg—common enough in the wards for patients with cutaneous diseases in the Philadelphia General Hospital—but because it is advisable to show the beneficial effects of red cell blood paste. The patients were almost well of their ulcers when my service terminated in September. The second patient had an ulcer the size of one's palm on the dorsum of the right foot when first seen, in July 1944. The first patient was seen about that same time. The use of a patient's blood for the treatment of ulcers was originally suggested by Dr Naide at the University of Pennsylvania. Some months later, Drs Murray and Schar suggested the use of a red cell paste. I have prepared such a paste, somewhat modified, using type O cells for a paste prepared with powdered tragacanth and a 1:1,000 solution of phemerol chloride. The exact formula was as follows: A paste was prepared by powdering 25 Gm of powdered tragacanth into 75 cc of 1:1,000 solution of phemerol chloride. This mixture was allowed to jell, 25 Gm of the jelled tragacanth-phemerol chloride mixture was then added to 500 cc of red blood cells (type O) precipitated to the bottom of a flask. The bottle was thoroughly shaken and then placed in a refrigerator at a temperature of 3 to 5 C until ready to be used. The paste was smeared on the ulcer daily or every other day and allowed to dry. I believe that this red cell blood paste is of value in the treatment of nonspecific ulcers. I would not expect it to be of any value for a tuberculous or a syphilitic ulcer or even for a diabetic ulcer in a patient in whom the blood sugar level has not been brought down. It is certainly worth a trial for the majority of ulcers of the leg, which are, as is generally known, usually nonspecific.

DR MARJORY K HARDY The Mayo preparation is available through the Baxter Laboratories in Chicago.

DR SIGMUND S GREENBAUM It is important to use type O cells because they are closer to those of most bloods. It will keep indefinitely at 3 to 5 C.

### **Pemphigus, Apparently Favorable Response to Sulfadiazine Therapy** Presented by DR FRED D WEIDMAN, DR BERTRAM SHAFFER and DR SIMON KATZ

J S, a white man aged 64, senile and somewhat emaciated, presents several crusted and bullous lesions on the extremities. The mucosae are at present uninvolved. The patient was successfully treated for pemphigus from January to May 1944 with sulfadiazine. He was readmitted to the hospital on June 13, 1944, in relapse. The Wassermann reaction of his blood was negative. The blood chemistry, blood cell count and urinalysis were within normal range. He was given sulfadiazine by mouth, 1 Gm three times a day, and boric acid ointment and sulfadiazine ointment (5 per cent) locally.

## DISCUSSION

DR MEYER L NIEDELMAN I suggest the use of acetarsone. I have a clinic patient and also 1 in private practice who have responded well to acetarsone therapy.

DR CARMEN C THOMAS I remember this patient on a previous admission, and at that time he had lesions of the mouth which he does not present now

DR REUBEN FRIEDMAN I presented before this Society several years ago a patient with pemphigus who was treated with sulfadiazine and vitamin D for about a year She has had no recurrence of her bullous lesions in the past two years

## METROPOLITAN DERMATOLOGICAL SOCIETY

Royal M Montgomery, M D, *President*

James Lowry Miller, M D, *Secretary*

Nov 20, 1944

**Alopecia Cicatrisata** Presented by DR RICHARD J KELLY

C E, a white woman aged 32, had noticed a loss of the hair of her scalp since the age of 15 She dates this loss of hair around the time her menses began The menses have been regular The family history contains nothing unusual The patient's general health has been good The major loss of hair had been over the vertex At the present time, there are scattered tufts of hair surrounded by flat white scarred areas There is no evidence of infection in the hair follicles The blood count and basal metabolic rate were normal The serologic reaction for syphilis was negative

### DISCUSSION

DR JOSEPH C AMERSBACH I am not certain of the diagnosis I think that the diagnosis rests between lupus erythematosus and folliculitis decalvans I should like to hear from Dr Kelly as to whether there has been much activity of the eruption while under observation

DR J LOWRY MILLER I favor a diagnosis of folliculitis decalvans I thought that I saw evidence of scaling around some of the follicles on one side of the scalp I do not find any lesions of lupus erythematosus elsewhere

DR GERALD F MACHACEK I think that it is a case of pseudopelade following folliculitis I forgot to look at the patient's nails I think that it should be done to rule out the possibility of favus

DR LESLIE P BARKER The areas of alopecia present definite scarring with a folliculitis at the periphery of the lesion I think that this is a case of folliculitis decalvans

DR MAURICE J COSTELLO I agree with the diagnosis of alopecia cicatrisata

DR ROYAL M MONTGOMERY Folliculitis decalvans and alopecia cicatrisata are closely related If there is activity about the follicles, folliculitis decalvans should be the diagnosis, and if not, alopecia cicatrisata This is not mycotic in origin I agree with the diagnosis as presented

DR RICHARD J KELLY I presented the patient because I did not find any evidence of infection on careful examination Also I could not find any evidence of lupus erythematosus either in the mouth or elsewhere There appears to be no neurogenous factor present I inquired into the patient's background carefully and found that she is a very stable woman, and in the absence of infection I felt that alopecia cicatrisata was the proper diagnosis

**Neurodermatitis Improved by Injections of Histamine Phosphate** Presented by DR MAURICE J COSTELLO

A B, a woman aged 56, has had a generalized eczematous eruption for fifteen years

## DISCUSSION

DR JOSEPH C AMERSBACH I thought this case interesting, particularly from Dr Costello's observation that the eruption has shown such a decided improvement with the use of this medication. In my experience, the use of histamine has not resulted in much improvement in this type of case. My experience in the use of histamine, however, has not been extensive.

DR J LOWRY MILLER It has been my impression, as it has been that of Dr Amersbach, that histamine phosphate is generally not of particular value. About one month ago I saw a patient who had a widespread dermatitis following four hundred scratch tests in four days. While under treatment with histamine phosphate the eruption completely cleared. I attributed most of the recovery to the removal of the offending allergens. Cold urticaria, in my experience, is influenced favorably by treatment with histamine.

DR GERALD F MACHACEK It is most interesting that after injections of histamine the patient should have such a remarkable improvement, particularly when one recalls that many allergic manifestations are considered as being due to the effect of histamine.

DR THOMAS N GRAHAM Eruptions of this type are resistant to treatment, and I think that any therapy which may possibly be effective is worth a trial. I should like to ask Dr Costello what dosage of histamine phosphate he used and at what intervals he gave the injections.

DR RICHARD J KELLY There was a similar case that came to my attention at Vanderbilt Clinic. The patient had been treated previously in Cleveland, Chicago and Philadelphia. One of the residents began injections of old tuberculin (1:100,000) twice weekly in doses ranging from 0.1 cc to 0.6 cc. The patient responded within three months and is now cured. I suggest that that be tried with or without sulfonamide therapy.

DR J P BERGLER (by invitation) I had the opportunity of attempting histamine phosphate desensitization of 4 or 5 adolescent atopic patients for a period of one month's hospitalization. This program was continued for about two months after discharge, and, except for the moderate improvement to be expected in association with hospitalization, no appreciable benefit accrued from this effort of desensitization. However, the use of histamine azoprotein as a possible nonspecific desensitizer in chronic contact allergy, I felt, had a definite value, not so much in the curative sense but, rather, to lower perhaps the patient's sensitivity so that he or she could continue the daily pattern of life in spite of unavoidable environmental allergens.

DR ROYAL M MONTGOMERY At St Luke's Hospital, I have used histamine phosphate for 2 patients. Both had dermatitis exfoliativa. The eruption of 1 followed bismuth therapy and that of the other followed use of silver arsphenamine. One patient greatly improved, and the other showed slight improvement following histamine phosphate. In the Negro woman, who did not improve when the dose was increased to 0.2 cc, definite dizziness and nervousness appeared.

DR MAURICE J COSTELLO An internist at Lenox Hill Hospital who has had excellent results in the treatment of asthma with injection of histamine phosphate begins with very small doses. Dermatitis exfoliativa following arsphenamine has been treated successfully with histamine. In the past three months I chose several patients with severe neurodermatitis and treated them by injection of histamine three times a week. I have thus far been impressed by the favorable response of this dermatosis to histamine therapy. This woman is not cured, but she volunteers the information that she is much better. I think that histamine is worth trying in a larger number of cases. It is somewhat dangerous to use, because reactions may be severe. One should proceed cautiously and administer extremely small doses, e.g., 0.025 cc of histamine phosphate. If 0.0025 cc is given, it is a safer dose. I think that it should be given every day or three times a week to begin with.

**Residual Eruption Following Acute Dermatitis from Oil** Presented by  
DR LESLIE P BARKER

M K, a worker in a wai plant, was first seen by me on Aug 7, 1944, at which time he gave a history of having had a dermatitis on the trunk, arms and legs of fourteen months' duration. He had been treated by various physicians with local medication and had received about ten roentgen ray treatments over the affected area. He handled various greases and cutting oils in his work.

When first seen the patient had an acute, red, oozing and crusting dermatitis on the trunk and arms and to a lesser degree on the face, scalp and legs. It cleared within a few weeks with local soothing lotions. The patient's skin is apparently sensitive to all creams or greases.

The present residual eruption has persisted and itches intensely. It consists of recurring vesicles and numerous scratch marks about the wrists, extensor surfaces of the arms, face and scalp and, to a lesser degree, on the buttocks. The itching is apparently intense.

The patient is presented to show an eruption simulating, at least by the distribution, dermatitis herpetiformis as the residuum of a contact dermatitis. He is also presented for suggestions as to therapy. Patch tests done with two of the oils that he handles elicited positive reactions.

DISCUSSION

DR RICHARD J KELLY I agree with the diagnosis. I think that this patient is one of those persons who previously were not in contact with various oils, and have recently been going into occupations involving such contact. I think that this eruption is an oil folliculitis. The eruption can be controlled by applications of white lotion.

DR MAURICE J COSTELLO There is nothing now which to my mind suggests folliculitis. I think that the patient has some eczematoid reaction at the present time. Whether the oil was responsible or not would be difficult for me to say. But it is not the conception I have of dermatitis due to a cutting oil. It is the type of eruption I should expect to respond to roentgen rays. I think that that already has been tried.

DR JOSEPH C AMERSBACH The condition of this patient strikes me as being the residual eruption. I do not think that it is uncommon to see in eruptions of this kind development of a superimposed neurodermatitis which may go on for months as a result of the primary irritant. Persistent treatment which may require frequent changes of lotions and ointments, and roentgen ray therapy is necessary to get an eruption such as this under control.

DR J LOWRY MILLER Observation of the patient tonight suggests a contact dermatitis, as the exposed areas are those chiefly involved. On the other hand, he has been away from work for one year, and the history states that he had eruptions on the sacrum and shoulders, suggesting the diagnosis of dermatitis herpetiformis. I think that a therapeutic trial of sulfadiazine is justified.

DR THOMAS N GRAHAM I agree with Dr Costello that this eruption does not appear to be a dermatitis due to cutting oil, particularly since the patient had not been exposed to the oil for a long time. Dermatitis herpetiformis should be considered in this case. I believe that a biopsy would be helpful in establishing the diagnosis.

DR LESLIE P BARKER When I first saw this patient he had an acute red oozing dermatitis involving the trunk, face and arms. He had received twelve roentgen ray treatments on the areas and had used various medications locally. I have not been able to learn the nature of his previous medication. When the acute phase of the eruption subsided the present residual itching remained, involving the extensor surfaces of the arms, the lower part of the back, the buttocks and the scalp. A few vesicles developed in these areas and the itching has been intense.

The eruption certainly resembles dermatitis herpetiformis. Because of this similarity I prescribed sulfathiazole, 4 tablets a day for a period of ten days. There was no improvement, and the eruption was not made worse. Roentgen ray treatment does not give him any relief. All oily medicaments aggravate the eruption.

## DETROIT DERMATOLOGICAL SOCIETY

### SYMPOSIUM ON INDUSTRIAL DERMATOSES

Frank Menagh, M D, *President*

Robert C Jamieson, M D, *Chairman*

Hermann Pinkus, M D, *Recorder*

*Nov 21, 1944*

### Late Effects of Scalping Presented by DR ROLLIN H STEVENS

The patient is a white woman aged 64, whose whole head is cicatrized with shiny white scar-tissue except for an area of about 78 cm on the crown of the head. Here, there is a papillomatous, ulcerated and crusted lesion, suggesting basal cell epithelioma.

NOTE.—On Jan 2, 1945 a biopsy of one of the papillomatous lesions showed only an inflammatory process.

#### DISCUSSION

DR R H STEVENS In the fall of 1890, when I was ambulance surgeon at Grace Hospital, I was called out to a mill on the west side of Detroit and found an 11 year old girl who had got her hair wound around a shaft and had her scalp torn off. The scalp was lying on the floor in the chaff and dirt, which had been mixed in with the under surface of it in such a way that it was impossible to get the dirt out. The scalp was torn off, including the eyebrows, the right ear and a portion of the right cheek, the right side of the neck adjoining the scalp and the back of the neck within 1 inch (2.54 cm) of the scalp. The periosteum of the skull was included, from the middle of the forehead clear back to the border of the scalp posteriorly and laterally from just about the meatus of the right ear to about 2 inches (5 cm) of the left ear. I cleaned the scalp as well as I could and attached it, but it became necrotic and in a few hours had to be removed. I tried a large graft from the sister who is two years younger and applied it to the surface where the periosteum was not removed, but not much of it grew and from time to time I tried various kinds of grafts, taking a considerable number from my own arm, which were large, shaved off with a razor and sewed up again. Later, in 1904, I took a large number of grafts from the patient's own arms and distributed them over the sides of the head. These grew well. The technic was not too aseptic in those days. The outer table of the skull gradually sloughed away during a period of about four years. The family moved out of the city, and I lost track of the girl. When I saw her last she was anemic, and it did not seem to me that she could survive long.

However, on Oct 25, 1944, a 64 year old woman came into my office and announced that she was the girl who had had her scalp torn off in the fall of 1890, when she was 11 years old. I learned that she had been exhibited for months after I saw her last by a company manufacturing a cure-all salve. The grafts had been able to grow and cicatrize over the crown of the head.

The case is interesting from several standpoints.

1 There is danger of scalping when long hair gets wound around rapidly revolving shafts in industrial plants, an accident which has happened, I believe, many times.

2 The facts are that after skin grafts were applied to the borders of the lesions on the scalp and the outer table of the skull had been removed healing over the entire vertex had taken place and lasted over fifty years, until now a chronic papillomatous ulcerated and vesicular dermatitis has appeared

3 The patient is married and had three children, two of them, aged 29 and 31, living, and 1 grandchild, she is in good health, while all other members of the family—father, mother, sister and brother—have died

4 Roentgenologic examination reveals fairly normal tables of the skull

DR R C JAMIESON There were many bony protuberances, and I think that it is easily possible that after this length of time some malignant growth is developing in these areas. It happens many times that girls are literally scalped, and this seems to be a real occupational hazard

INDUSTRIAL SURGEON A I have had little experience with that type of case. Most of the women who work in the factories now have shorter hair than this 11 year old girl probably had in 1890, when she was hurt. Furthermore, great care is exercised to see that women wear some sort of garment that will protect them against being caught in moving parts. Also, there is much less overhead machinery than there used to be. There was a time when everything was run by overhead pulleys and belts, now nearly every machine is a unit unto itself, and opportunity for accidents of the sort mentioned is pretty well past. Notwithstanding this fact, though, cases do occur, but I have not heard of one in which the damage was so severe as in this one

In the past two years I have had 3 cases in which grinding wheels exploded, and, as bad luck—or good luck—would have it, a piece grazed over the scalp of a workman, taking out the hair right down to the scalp without any actual injury to the skin. In 2 of those cases there has been no regrowth of hair. I should like to ask what has gone on that has kept the hair from growing back in 2 of 3 cases in which loss of hair was occasioned by flying pieces of grinding wheel

DR R C JAMIESON What was the appearance of the skin? Was it smooth and soft, as in alopecia areata?

INDUSTRIAL SURGEON A The hair is normal everywhere else. In this definite area there is stubby hair, it is not completely bald, but the hair will not grow

INDUSTRIAL SURGEON B In 1 particular case I recall, the chief trauma was not physical at all. The patient was much worried about the hair not growing back. There have been several exhaustive examinations made, and it has been decided that the injury was probably psychoneurotic in character. This person is getting his hair back now fully

#### Contact Dermatitis, Caused by Zinc Chromate Paint Presented by DR GEORGE VAN RHEE

G D, a white woman aged 26, has had an eruption on the hands and arms for about one month. She has been employed as a driller and riveter since June 1944 in a place where she has contact with zinc chromate paint

The examination shows a diffuse erythema in patches on the extensor and flexor surfaces of the arms, being particularly severe in the cubital spaces. There are a few small patches on the dorsum of the hands

#### DISCUSSION

DR R C JAMIESON I should like to have some of the industrial dermatologists add to the question of whether some of these eruptions are due purely and simply to the chromate with which the aluminum is painted or whether some are due to the mechanical irritation of fine particles which land on the skin and become

embedded, causing trouble in that way I have seen both types, and I think that there is a distinction between the two I believe that clinically I am able to tell the difference

INDUSTRIAL SURGEON C I try to talk patients out of the notion of aluminum poisoning as much as I can and assure them that a great deal of their trouble is due to personal hygiene Then, if I cannot do that, I try to find some source of chromate I have not seen any from aluminum dust, although it is a current belief in the factory that that is the cause of poisoning

DR R C JAMIESON I think that most physicians believe that aluminum itself is nonirritant and the only way it could cause dermatitis is through contact with small irritating particles

DR GEORGE VAN RHEE This type of dermatitis seems to occur in certain plants It occurs in all plants in which airplane wings are worked on, and it occurs primarily where zinc chromate paint is used Personally, I have never seen a positive reaction to a patch test with straight aluminum I believe that one can get a positive reaction to a patch test with an alloy containing magnesium There is a dermatitis which can be contracted from aluminum covered with an oil (commonly called "fish oil") This produces a more or less diffuse type of dermatitis The particular type of dermatitis in the case I presented today is a blotchy type, it is diffuse in the area itself It is circumscribed, and it occurs only in certain areas—on the back of the hands, on the forearms, on the lateral surfaces of the neck (frequently in the postaural folds) and on the eyelids It occurs much more frequently in women than it does in men Now I understand that a large amount of this riveting and drilling on the airplane wings and fuselage is done by women It also seems to occur more frequently when the drilling is done overhead In addition, these women also get a dermatitis from repairing of parts As I understand it, when any parts or materials are injured or defaced they are marked with paint, and then these girls are required to remove this paint when repairing them That is a different type of dermatitis, and it looks much like that in case 3 presented today It is a vesicular dermatitis There is another process in one of the Carboloy plants where much the same type of dermatitis is contracted, which at the beginning I thought was seborrheic dermatitis, and I diagnosed a number of the eruptions as such until I kept getting a good many similar cases Finally, I decided that it was not seborrheic dermatitis after I performed patch tests on some of the patients and got a positive reaction I noticed this dermatitis in cases in which the women wore loose blouses

DR A E SCHILLER I agree more or less with Dr Van Rhee I have seen a good many of these cases, and I have been interested enough to try to find out what part of the aluminum working processes might be involved in this dermatitis It did not seem likely to me that the chromate paint itself was the main factor, and one of the company physicians sent me a pamphlet on chromic acid and the oxidizing of aluminum Apparently, the specifications by the government call for protective treatment of aluminum and aluminum alloys by an oxidation process in which chromic acid is used Thus, it seems altogether probable that one can get a chromic acid type of dermatitis from an aluminum that has not been painted with zinc chromate paint, and I think that this is probably one of the features which has been overlooked in the study of aluminum as it is used today in the manufacture of airplanes

Now, in reference to stainless steel and Carboloy, I agree with Dr Van Rhee's statement wholeheartedly I have seen dermatoses that vary from a patchy vesicular or a patchy, scaly dermatitis to one involving practically the entire body and looking exactly like parapsoriasis The first ones seen I diagnosed as parapsoriasis and labeled them as nonoccupational I have seen 6 of them since, and they differ from parapsoriasis in that they will clear up readily when the patient is removed from the occupation, together with the use of any mild oily



preparation on the skin I think that in all probability some dermatologists have been overlooking these eruptions just as I did and have been calling these cases nonoccupational I think that the ideas on aluminum, stainless steel and Carboloy in the industrial processes will have to be revised somewhat

DR GEORGE VAN RHEE I agree with what Dr Schiller has just said In the same plant 2 or 3 patients who had no contact with zinc chromate were sent to me, but there was anodizing and these patients presented much the same picture as the others that I have described

INDUSTRIAL SURGEON A I have had well over 100 cases of the sort which Dr Van Rhee mentioned first I am not so sure that all this is due to the zinc chromate Over and over I have taken pure zinc chromate in powder form and have attempted to produce something artificially, even on people who had an eruption that might have been due to the zinc chromate The difficulty in this particular situation began at a time shortly after the federal government imposed on paint manufacturers the use of a certain toluene substance I, at least, believe that some of these dermatoses are not due to zinc chromate, but are due to the half-dry paint that is present on the substances with which these factory people work If one could be right in the department and watch these people, one would find that nearly all of them have a little bottle of some liquid They call it "thinner," although it may not always be thinner They are continually "touching up" something with this liquid When a few rivets are put in, replacing some that were removed because of defects, the workers have to take this paint and touch up the newly applied rivets I am disposed to believe that the majority of the dermatoses I have seen are due to the liquid portion of the paint rather than to the pigment or the zinc chromate part, although I do not deny that zinc chromate may occasionally cause dermatitis As to the question of aluminum or aluminum alloy causing dermatitis, there is one job that does not require painting and one or more jobs that require painting Ninety per cent of the difficulties have occurred in connection with the paint jobs, and most of them have arisen in circumstances in which there was exposure to liquid portions of the paint

Getting over to the matter of stainless steel, I should like to inquire if any of you gentlemen know whether there is a fluoride content in stainless steel If so, that may be the specific cause of the dermatitis At any rate, a fair amount of dermatitis is now being seen in connection with stainless steel that I believe to be due to fluorides

DR GEORGE VAN RHEE I have the chemical analyses or metallurgic analyses of one particular company, and there is no toluene or derivative of toluene listed so far as I know on that particular subject, and in their analysis of stainless steel there is no fluoride mentioned in the data

DR FRANK MENAGH I should like to say that I have had the same experience, except that if clean chips are taken there will not be much of a reaction, but if the chips around the machine are picked up positive reactions are elicited to patch tests I think that it ought to be remembered that other things, such as ordinary machine oil, lubricating oil and grease, are sometimes mixed with the chips and are a real cause of dermatitis

#### Contact Dermatitis Due to Frequent Contact with Thinner Presented by DR GEORGE VAN RHEE

N S, a white man aged 44, has had an eruption on the hands since July 20, 1944 He is a crater and works with tar, which he removes with thinner

The first examination revealed a definite erythema, with vesicles involving the palms and the dorsal and lateral surfaces of the fingers This was followed by exacerbation and spread to both arms, particularly the cubital spaces A macular eruption involving the body followed, which I feel is due to absorption

## DISCUSSION

DR GEORGE VAN RHEE One thing is certain The patient has a contact dermatitis As to the definite causation, he could get this dermatitis from "thinner," he could get an irritation from tar or he might even get an irritation from wood So far as I know, there is no preservative used on this wood The patient admits that he has been in the habit of removing the tar from his hands with the "thinner," which, of course, can produce a severe dermatitis

DR H L KEIM This type of picture is being encountered with fair regularity, since these boxes are being packed and shipped to the South Pacific, and, as Dr Van Rhee says, it is not always possible to tell immediately which one of the factors is involved, but the type of contact dermatitis shown here is frequently seen in the packing end of the export trade

DR A E SCHILLER I was inclined to believe, because of the diffuse distribution of the lesions, that this might be an allergic reaction to inhaled wood dust I saw a case similar to this three years ago I could not tell it from others of the inhalant allergies, but, with the wide distribution that is presented here and with the evidence of toxicity that accompanies it, I should like to offer a diagnosis of a wood dust allergy

DR GEORGE VAN RHEE Most of these men are not exposed to dust, they are just exposed to packing that is already made

DR R C JAMIESON I think that the discussion in regard to the components of some of these irritants, the various ways in which these paints are made, the specifications and things of that sort would serve to point out many of the difficulties under which physicians labor in trying to arrive at definite diagnoses of the specific substances causing the trouble I think that the industrialist realizes that a physician cannot immediately on seeing a patient say what is causing the trouble It is true that many of these patients will react positively to patch tests with some of the things that are used in their occupations and yet they may have a dermatitis due to something entirely different I think that this has been the experience of all of us Now, if any one would like to answer the question as to whether a dermatitis such as this man had would prevent him returning to the same occupation or not, I should like to hear it

INDUSTRIAL SURGEON D I think that in most cases the answer is obtained only after the man goes back to work and continues without trouble or gets into trouble again If the trouble does develop again, then he should not be exposed to the same particular hazard

DR H L KEIM In this particular case, it was apparently Dr Van Rhee's opinion that most probably this was due to "thinner" which the patient used to remove the tar I think that this is the precipitating factor many times and that often the factor will be in the way the worker cleanses his hands If this is presumed to be the case, then reeducation of these workers in the care of their hands might permit them to go back to their occupations If the dermatitis comes back after this regimen, then I think that the worker should not continue that work, because it seems to prove to me that it has something to do with that particular vocation rather than other associated factors

DR GEORGE VAN RHEE After this attack developed in the patient and prior to the time I saw him, he went to see his own physician, and the physician applied some soft ointment I do not know what it was, but I suspect that it was sulfathiazole ointment which caused the severe exacerbations on his arms and probably accounts for much of the trouble he presented in addition to the original dermatitis

DR FRANK MENAGH Once a man has had a dermatitis as severe as this man had and has had enough absorption so that a secondary eruption develops, he frequently undergoes successive cycles, even though he stays away from work, when he returns to work, he may well be found having another outbreak

### Tattoo-Like Staining Following Occupational Dermatitis Presented by DR ARTHUR E SCHILLER

A K, a single white woman aged 53, has worked for a considerable period in a war production plant. She was first seen Sept 4, 1943. Until April 1943, the patient worked in a mixture containing 80 per cent kerosene and 20 per cent turbine oil. At this time an eruption developed on the back of her hands and arms, which began to get red and scaly. She used soap powder and a liquid type of soap dispensed at the factory for cleaning. After the development of her dermatitis, she was removed from the work of testing seats and gages and was given a job drilling holes, in which she used Sultex-B (a cutting oil) and 50 per cent turpentine. She stated that she did not come into direct contact with the oil but she did come into contact with the "fumes and possibly a fine spray."

After a number of weeks at this occupation, a dermatitis of the face, neck, arms and hands of varying intensity developed. She was given patch tests with all the ingredients with which she worked. All the laboratory tests elicited negative reactions.

Pigmentation and the residual inflammation was arranged in a peculiar manner, being retiform in character, and the follicular openings were capped by tiny brown scales. The inflammatory condition improved rapidly with a mild sedative treatment, and there has been some improvement in the pigmentation.

#### DISCUSSION

DR A E SCHILLER I thought that this was interesting not only from a clinical angle but from its medicolegal possibilities. The lesion presented itself as a tattoo-like staining, and for a number of months it seemed impossible for the patient to get any relief from it at all. I think now that she may possibly get an improvement. She had a positive reaction to a patch test with 10 per cent turpentine in soybean oil and a negative reaction to a test with the soybean oil itself.

DR FRANK MENAGH I had a similar experience with a young woman who while working in oil became warm and wiped her face with her greasy hands. An acute dermatitis developed on her face, and after this a really bizarre pigmentation developed. So far as I could tell, it was identical with Riehl's melanosis, which has had an interesting history. After the last war, Riehl, a German, saw a good deal of this pigmentation and thought that it was due to poor diet, however, it has been pretty well shown that this was not true, and, specifically, there have been cases shown to be due to an oil that was contacted in spinning jute, as I recall, hence contact with oils of various sorts is an etiologic factor in producing pigmentation in some of these cases. The young woman I mentioned took a number of months to begin to show any improvement so far as the pigmentation was concerned, but it is gradually disappearing now.

### Persistent Contact Dermatitis Presented by DR ROBERT A C WOLLENBERG

A white man, aged 46, had never had an eruption of any kind prior to the beginning of the present attack, there was no history of eczema or dermatitis in childhood. This eruption began on the upper half of the body about October 1943, while the patient was working at a machine which splashed a cooling mixture ("soda water") and caused his clothing to "smell of oil." However, he continued to work for a time, but, the eruption becoming more severe, he was transferred to another machine in his factory, which dripped oil from above him. The eruption lessened for a while, then gradually grew severer, especially on the shoulders, arms and upper part of the back. However, he continued to work.

In January 1944, he injured a wrist. The injury was diagnosed as a sprain, and a "liment" was applied at the factory, after which the cutaneous irritation spread rapidly. The patient was treated by a dermatologist, with "no improvement" after he had spent one month in a hospital (April-May).

Examination on July 8 revealed a general dermatitis, nearly all the skin being involved to some degree with erythema and branny scaling, a moderately severe dermatitis being present over the scapulas, cubital spaces, flexor surfaces of the arms and forearms, extensor surfaces of the forearms and hands, inner and posterior surfaces of the thighs and legs and in the popliteal spaces. The more involved areas showed moderate lichenification. His general physical condition was good, without abnormalities, except for some carious teeth, which were later removed.

Quitting soaps of all kinds and using a mild crude coal tar ointment caused a moderate improvement by early September. However, there were a moderate increase in signs and more itching with weeping and swelling of the external ears in late September. Since that time there has been considerable variation in the degree of the eruption, which never entirely disappeared. A diet low in fat and 150,000 U S P units daily of vitamin A appear to have had no effect on the eruption, nor have there been any definite changes as the result of injections of sodium cacodylate or sodium thiosulfate in usual doses. Mild crude coal tar ointment and boric acid ointment appear to have caused some improvement. "Soothing" lotions have usually increased the itching.

At present the patient has a moderate erythema of the upper part of the back, slight crusting on one ear and mild to moderate lichenification of the arms, forearms and large flexures of the extremities. He still suffers much from itching.

#### DISCUSSION

DR R A C WOLLENBERG: I see a number of these cases, and the thing that impresses me in particular in connection with many of them is the fact, one which was brought out some moments ago, that the specific cause of the irritation is difficult to determine, at least for physicians in private practice.

I was asked the question, "What is soda water?" My impression is that it is a complex compound or mixture that often is made of all the junk oils in the factories. There is probably a fundamental ingredient in what is called "soda water" in the factories, but I myself have never been able to identify it because, from what I have learned, nobody really knows what it is. So I should be glad to have your answer to that question.

Unfortunately, a private physician is not in the same position as industrial physicians are. It is only with a great deal of difficulty that some of these compounds or materials which may be suspected may be obtained, for the reason that the "boss" will not give them to the employees for patch tests because he fears legal consequences, at least so I have often been informed. The only thing that the patient can do is to filch them. If he cannot obtain them, he has one of his friends get them for him. This is not a proper or legal source of information, for most of it has to come through channels of that nature. I have made it a point frequently to inquire as to the nature of the various compounds which the workmen handle, and I have yet to get one exact answer to my question from any of the manufacturers. They simply will not give the information to a private practitioner, or they do not have it. What the oil was to which the patient was exposed I do not know. His dermatitis lasted over a couple of months, during which time he was operating this machine. Finally, it got so bad that he was taken off the work, and he then promptly recovered. He was put on another job, in which he was again exposed to oil but of a different type. Again the same thing happened, on top of which came the sudden explosive eruption which resulted from the contact with liniment or whatever it was that had been applied to his wrist. These cases are seen over and over again. Once in a while one can get a clear-cut history.

I mention 1 case, that of a man who worked in the box shop. He had been a carpenter all his life, he never had an irritation before. After he had been in the factory for a period of three or four weeks, a dermatitis of the hands appeared,

and it grew worse and worse. He had a very severe dermatitis, with scaly, oozing lesions all over the face, shoulders, back, arms and forearms, as well as on the hands. Fortunately, he was in a position to bring me the contacts, which happened to be pine wood, hemlock wood and nails. I learned that these nails were covered with a rust-proofing material. I performed patch tests with these three articles, and there was a severe vesicular reaction to the rust-proofing material. I did not put much on, but he had just as much of an escharotic reaction from that material as he would have had from an application of pure phenol. Pine wood gave a 2 plus reaction, the hemlock-tested area was moderately red, but less so than that tested with the pine. Eventually he went back to work, but he does his work with leather gloves and he is having no trouble. There is a case of specific allergy, there is a specific effect, there is a patient who got well through proper protection.

The point I want to make is this. You gentlemen in the factories, knowing the contents of these complex compounds and knowing whether a thing contains fluorine or nickel or whatever it is, are in a strategic position to run these things down, while the private practitioner, for obvious reasons, is not permitted to do so.

**INDUSTRIAL SURGEON A.** In industry any cutting compound is called "soda water" by the workmen. It is not soda water in the sense that it contains an alkali. When such cases get into the compensation courts, the lawyers who represent these plaintiffs are prone to build up their cases on the grounds of the alkali being the responsible cause. Such is not the case. There was a time when sodium carbonate was widely used in connection with oils in order to emulsify them. Under present speeds and types of operation, that sort of coolant would no longer work. However, there are still white coolants, the things that are called "soda water" by the workmen. These are water-soluble oils, and many of them contain sulfur. They are either sulfonated, sulfurized or sulfur treated or something of that sort, and it is my belief that a great deal of the difficulty is related to the sulfur content. It so happens that these water-soluble oils make a fine medium for the growth of bacteria. As the bacteria grow, apparently the sulfur decomposes from its original form to another form that is much more irritating. If a man brings down to the office a sample of oil for a patch test and if it stands around for a couple of days before it gets to the office and the physician keeps it another couple of days, it is almost a certainty that decomposition will have taken place so that there will be a positive reaction to the patch test when there might not have been a positive reaction if the material had been taken right off the machine. So far as I know, in the factories at the present time no alkalis are added to these coolants that, properly speaking, should be called water-soluble oils. Some of them, instead of being treated with sulfur, are treated with chlorine, so there is the double exposure feature of chlorinated oil.

And lastly, any time a dermatologist would like to know what is in any particular coolant in our factories, call me. Nearly always I shall be able to give you some nearly exact information, and I shall be glad to do so.

**DR. A. E. SCHILLER.** I should like to contradict one statement. I have yet to find a plant that is not willing to cooperate with information and material for examination and patch tests which would help in determining the possible cause of dermatitis. I have received nothing but courtesy from the first aid departments. A good many of the men in charge and a good many of the nurses in charge have gone distinctly out of their way to give me information that I asked for. I should hate to feel that an impression is left that any one of the plants today, or at least that most of the plants today, are in the habit of refusing a physician material to conduct his tests.

**INDUSTRIAL SURGEON E.** I might add a thought. Probably if the man himself tries to get the material, he does run into difficulties, whereas if the physician would contact the plant physician he would get the information.

**DR. R. A. C. WOLLENBERG.** Four weeks ago I had occasion to write to two different plants, one of which gave me the answer that they received the material from some one else and had no idea what was in it while the other gave no reply.

whatsoever Another plant told me exactly the same thing, that the suspected material was obtained elsewhere This has happened a number of times before The original manufacturers simply will not give an answer, and the plants using the materials themselves usually do not know what they are Small plants do not always have plant physicians

INDUSTRIAL SURGEON B When a person in the plant comes in with a dermatitis, I try to be fair with him all the way through A person who works in a factory oftentimes feels certain that any eruption that develops is of factory origin If there is a reasonable doubt that the man's occupation had something to do with his cutaneous disease, I often give him some symptomatic treatment, if the results of patch tests are negative, I try to consider what he might be contacting at home—cleaning materials or gardening materials, cosmetics and cleaning materials pertain chiefly to women If I feel sure that the disease did not originate in the factory, I refer the patients to their own family physicians, and if the family physician feels that there is an industrial dermatitis the patient is sent to our own diagnostician and further tests are made As I have said, these people frequently feel that any condition that develops is due to the factory Sometimes they are truthful about that, at other times these persons, working for a corporation that has made and is still making plenty of money, think that they are entitled to anything they can get That attitude on the part of the workmen is, I think, rather pronounced

DR HERMANN PINKUS The fact that the man had an acute flare-up after he had liniment applied to his wrist is important I think that this gives a clue which one should follow, because in my experience it has cleared up some puzzling recurrences and exacerbations in such cases Patients will often contend that they have no contacts at all in their homes If their homes are looked over it will be found that their bedrooms and medicine cabinets are stuffed full with liniments, nose drops, foot balms, perfumes and all kinds of patent preparations which have one thing in common—they contain oil of eucalyptus, methyl salicylate or similar essential oils I may be wrong, but I think that one can group all these oils together They seem to have a certain group specificity in their action on the skin I believe that if the homes of these patients are not investigated thoroughly, the patients will often not admit that they have contact with such preparations Sometimes the patient himself does not use them, but some member of the family does If one succeeds in convincing these patients that any contact with "smelling" substances must be avoided, and if their homes are rid completely of them, then often such puzzling, long-standing and always recurring dermatitides will surprisingly clear up

DR R A C WOLLENBERG Just to keep the record straight What Dr Pinkus says, I absolutely believe But, inferentially, it may be thought that Dr Pinkus may possibly be referring to the case I presented I do not think that he is, but I will say that if he is he is wrong in this instance The liniment was put on in the factory by the nurse He put nothing on, he was treated by the factory nurse and the physicians in connection with the plant

DR R C JAMIESON I think that the point Dr Pinkus brought out was amply demonstrated at a round table discussion before the Wayne County Medical Society, it was brought out time and time again that sometimes it really is necessary to live with the patient to determine what the irritant is

INDUSTRIAL SURGEON E Dr Wollenberg, in presenting this particular case, brought out the point that the man is unemployable I should like to get the feeling of the society on that, whether they think a man in this condition is employable or not

DR FRANK MENAGH I doubt that any plant physician would hire him

DR R C JAMIESON I should say that he would be employable if he could find some kind of employment in which he would have no contact with substances to which he is allergic There is also the question of whether there is something

in the man's background that would result in his having exacerbations based on a neurocirculatory disturbance. The persons of whom I speak had hands with the typical cold, clammy feeling peculiar to neurocirculatory disturbances, and it might easily be possible that no matter what he did he would still have some of these attacks.

#### **Dermatitis Due to Soap** Presented by DR HARTILR L KRIM

L G, a white man, aged 52 years, has been a gear cutter for eight years. His vocation has in no known way been changed. Two months ago an eruption first appeared on his feet and later on the hands. Pruritus is mild, and only ointments have been used. He presents an erythemasquamous dermatitis of both palms, particularly evident about the finger tips. On the feet, both heels and the lateral surfaces are involved in a finely erythematous desquamating dermatitis. A few fine vesicular lesions are evident on both hands and feet. There is no involvement of the interdigital webs or the nails. Further inquiry reveals the fact that within recent months his stockings have been cleansed with Roman Cleanser. In the absence of any clinical evidence of dermatophytosis, it was felt that this eruption represents a contact sensitivity to the bleach used in the stockings and accordingly is not occupational.

#### DISCUSSION

DR H L KLIM I brought along this man to exemplify one real difficulty that I encounter in establishing a diagnosis in these cases of eruptions on the hand. Many of them occur in older persons, who have been employed for a considerable period, and are frequently incorrectly diagnosed as ringworm. A number are, of course, the result of employment contacts, but also a great many result from contacts made outside the plant. I think that Dr Pinkus' point is especially well taken because the average patient who does not get well in a reasonable period will invariably try some home remedy. Frequently, the family physician is first consulted, and he, presuming that he is dealing with a fungous infection, prescribes ointment of benzoic and salicylic acid or some other irritating fungicide, with disastrous results. I am many times asked to decide whether or not these eruptions on the hands and arms are occupational in origin many months after they first appeared, the establishment of the diagnosis then I find extremely difficult to make, if I am to be fair to both parties concerned. This case of the patient with the eruption on the fingers, dorsal surface of the toes and heels does point out the fact that the employees frequently have dermatoses on their hands and feet which are not necessarily occupational in origin. This man informs me that his eruption started on his feet and that his stockings are washed with strong soaps with Roman Cleanser always added. It is my opinion that this eruption is a dermatitis venenata resulting from contacting these materials. It is my further opinion that this and many other eruptions on the hands are kept up with the use of alkaline soaps, notably medicated soaps and other irritants, and I feel that reeducation as to the care of the skin is an important part of the therapy. This patient has been unemployed for a period of six weeks but is not off duty because of the dermatitis but, as he says, "because of severe nervousness."

#### **Dermatophytosis of Hands and Feet** Presented by DR ROBERT C JAMISON

I L, a white man aged 30 years, worked in a defense plant from November 1942 to January 1944, being in contact with oil. A few weeks after starting work, his hands became reddened and edematous and a secondary pyoderma developed. Involution was almost complete after five to six months of local and roentgen ray treatment.

There has been no contact with oil for the past nine months, but he still has eczematoid patches on the palms and palmar surface of the fingers, with some small deep vesicles in and around the patches. Some areas are fissured and scaly.

without visible vesiculation Fungi were found microscopically Intensity is variable, usually greater in hot weather

**Atopic Eczema** Presented by DR ROBERT C JAMIESON

D P, a white man aged 31 years, works in a tool shop This patient was presented on account of having lesions on the forearms which could be confused with many lesions in that location due to occupational contact

The only lesions at present are bilateral and symmetric eczematoid demarcated patches on the inner and ulnar aspect of the wrists and forearms and a slight indefinite thickening and fissuring of the skin on the knuckles of several fingers The remainder of the skin is normal

His history shows that he has had atopic eczema for fifteen years and before being in the army had had contact with oil Lesions had been present on the ankles while he was in the Army, but the lesions on the arms and hands had not been bad at that time There is no contact with oil in his present occupation

DISCUSSION

DR R C JAMIESON The last 2 patients were presented partly with the object of getting some expression of opinion as to how dermatologists feel about these cases that were at one time compensation cases The patient still has lesions that he wishes to be considered compensable but which clinically are not those of the compensable disease at all I L has keratoses on the palms, patches of dermatitis which are demarcated with satellite vesicles in which fungi are found The great difficulty in these cases is to convince the patient that this is not the original disease, even though he has not worked at that particular job for many months and the lesions are not at all of the occupational type These people make, or try to make, a physician sign papers, and the lawyers in the case try to get a physician to say that it is still a compensable case, even after many months or even a year or two The question of the concomitant eruptions, fungous infections accompanying, preceding or following occupational dermatitis, makes one of the most complex problems that physicians have to deal with today and one which I think cannot be solved in any dogmatic way I think that each of these cases has to be judged on its own merits The man I presented is in a sales position at present, and yet he has these patches which he thinks are compensable The only thing I can do with him is to try to persuade him to the belief that these lesions are not compensable and that what he has now is in no direct relation to what he had before The other man I presented had lichenoid dermatitis in areas which might have been produced by occupation or might have followed certain occupations, such as coming in contact with or resting the arms on parts of the machine from which there might come a localized dermatitis

DR R A C WOILENBERG To enlarge the question, what is done in the case of the person who is known to have a fungous infection of the feet? He goes to work, and the hands get bad He quits work, and the hands get better He goes back to work, and the hands become bad He quits again, and the hands get better How about him?

DR R C JAMIESON I should be inclined to think that he had more than one condition He would have a residual fungous infection plus an occupational dermatitis The criterion of an occupational dermatitis is this Does it come on when the person goes to work? Does it clear up when he quits? Does it come back when he goes back to work?

DR LOREN SHAFFER I think that Dr Jamieson is to be complimented on his integrity and honesty in the management of this case in relation to the nonindustrial origin of the dermatitis I know that is a serious problem from an economic standpoint for the practicing dermatologist Here is a man who insists that his disease is industrial, and he practically puts the dermatologist on the spot, threatening that if he is going to get any pay he must support him in that particular contention



## NEW YORK DERMATOLOGICAL SOCIETY

Hans J Schwartz, M D, *President*George C Andrews, M D, *Secretary*

Nov 28, 1944

Multiple Pigmented Hairy Nevus (Melanocarcinoma?) Presented by DR  
A BENSON CANNON

J H, a boy aged 14 months, was seen in consultation Aug 8, 1944, for an  
opinion regarding treatment of multiple pigmented hairy nevus After a biopsy



Multiple pigmented hairy nevus

study of a specimen taken shortly after birth, a diagnosis of melanocarcinoma was made The patient is the only child of healthy parents, born at full term, normal delivery and apparently healthy except for numerous disseminated, brown, hairy, molelike lesions all over the body and extremities most numerous on the upper

part of the chest and on the sides of the face. A second biopsy, taken six weeks later from another hairy, pigmented lesion, was reported as confirming the previous diagnosis. The child has developed normally both mentally and physically, no signs of malignant growths have appeared, and as far as the mother and family physician know the child has been perfectly well in every respect. The lesions have not changed except that the hair in them has grown a bit longer.

Examination shows a well developed, well nourished and apparently healthy child of 14 months. There are extensive light tan to dark brown, pigmented, raised, hairy, molelike lesions scattered all over the body and extremities, varying from the size of a pea to a covering of the entire upper part of the chest, front and back, sides of the face and neck and the entire right arm to the elbow. There are palm-sized, smaller lesions on the outer aspect of each buttock and a bandlike wristlet around the left wrist. Some of the dime-sized to half-dollar-sized pigmented areas were macular and tan colored, with central pea-sized dark brown molelike papules in the centers. The hair in many of the lesions was from  $\frac{1}{2}$  inch to 2 inches (1.2 to 5 cm) long and fairly thick.

Two slides of the biopsy were presented with the patient. The diagnosis by both the dermatopathologist and the general pathologist at Columbia University was that of melanocarcinoma.

#### DISCUSSION

DR FRANK C COMBES. If the biopsy report, which has been verified by a dermatopathologist and a general pathologist, had not been mentioned, I should say that this was a simple pilopigmentary nevus of a benign nature, and I still think that it is. In this instance I think that the histologic diagnosis should be foregone and the growth considered as benign. I cannot see that this will make any difference, except insofar as prognosis is concerned. I do not think that it would affect the treatment, which would be to leave the nevi alone.

DR HOWARD FOX. I agree entirely with Dr Combes, both as to diagnosis and as to his recommendation that no treatment be carried out. I think that the idea of any plastic operation is out of the question at the present time. I should like to ask Dr Cannon whether he had in mind treating only the small possibly malignant lesions or the entire affected area.

DR RAY H RULISON. I agree with the previous discussers that the pathologic findings in this case should be disregarded.

DR GEORGE M LEWIS. It is difficult to carry out treatment with solid carbon dioxide, but if it is done cautiously and carefully one might obtain good results with the lesions on the face. I believe that the pigmented area should be treated with a large block of solid carbon dioxide, so that one would not get the patchwork quilt type of response. Any change would be a definite improvement in this case, in which such great disfigurement is shown. I am not impressed with the danger of malignant degeneration.

DR EUGENE F TRAUB. The report on the histology in this case is in line with a number of experiences that have been had in removal at random of pigmented moles of all types, which in most instances, from a clinical standpoint, were perfectly benign lesions. This was disturbing in the beginning, until it was found that apparently one could not invariably rely on the apparent suggestive changes frequently seen in the sections. Apparently, experienced pathologists in some instances are unable to determine whether lesions are benign or malignant. This is not difficult to understand when one stops to think that the changes observed microscopically in the benign junction nevus are in many respects similar to the changes found histologically in the malignant melanoma. One must therefore consider the clinical as well as the histologic data before coming to a decision as to whether the process exhibits true malignant characteristics or not. It will be recalled that I showed a young child with a pigmented hairy lesion on the cheek that had been removed by plastic operation and skin graft applied to the area. The report in this case was also malignant melanoma, and shortly after the operation pigmented areas appeared in the Thiersch graft. In addition nodes were

noted in the neck, and the possibility that the process was a true malignant and metastatic one had to be considered. The child was just seen today and has now been followed for several years since the operation. The nodes in the neck disappeared after tonsillectomy, and the pigmented changes in the graft have remained stationary.

It is my opinion that the lesion in this case probably was benign right from the start, despite all the peculiar findings, and I also feel that in Dr. Cannon's case these lesions are entirely benign. However, with that type of histologic report, I should certainly be against treatment with solid carbon dioxide because in any type of junction nevus the use of an agent that produces chronic irritation during a period is to be avoided. If anything at all is to be done in this case, wide excision should be practiced. I think that another point indicating the benign character of these growths is the fact that in three separate lesions, namely, on the cheek, the shoulder and the wrist, the same histologic structure was found. It would certainly be unique for a patient to show three primary melanomas originating from three widely separated points at the same time.

DR. GEORGE C. ANDREWS: I agree with Dr. Fox and Dr. Traub. I have seen only 1 patient in the last twelve years who has shown a melanoma on an extensive hairy nevus. This patient, an adult about 40 years old, had a bathing suit type of nevus, and a melanoma, which was eventually fatal, developed on the shoulder. Apparently it is difficult for pathologists to judge early changes in the melanoma. Dr. William B. Cole, formerly of Memorial Hospital for the Treatment of Cancer and Allied Diseases, who was interested in this subject for years, said that the clinical diagnosis was more important than the histologic diagnosis in cases of melanoma, and I believe that this is usually true. I agree with Dr. Traub that this lesion should not be treated with solid carbon dioxide, as this would not give a good cosmetic result. Plastic surgery might be worth considering, as large surfaces are now being grafted successfully.

DR. JOHN C. GRAHAM: I have had the same results as Dr. Traub has had in getting reports of melanoma on biopsy specimens when actually the lesion never developed into melanoma, and I finally gave up the idea of having pathologic reports in every case. It seems to be difficult for pathologists to distinguish between a melanoma and a benign nevus. In this particular case there seems to be no reason at the present time to suspect that there is a melanoma here. It may develop when the child becomes an adult but not now.

DR. GERALD F. MACHACEK: I think that the criticisms raised are valid. It is difficult to foretell what may develop. It should be borne in mind when a child with an atypical pigmented lesion is being dealt with and the question of a malignant growth arises that the lesion is apt to be not malignant. At least, it need not be considered as malignant, as it would be in the case of an adult. Even in frank melanomas—even in a tumor of the skin, for that matter—there is no recurrence until twelve to fifteen years later. I have had that experience before. I recall 1 patient with melanoma of the shoulder with recurrence and metastasis locally who is still alive, after many years. Evidently, the situation is not the same in a child as in an adult.

DR. MAURICE J. COSTELLO: I think that the mistaken interpretation is more likely to be made in lesions that have been treated by surgical diathermy. I have had several such experiences. I can refer to 1 patient in whom a coal black lesion developed in the center of a treated mole. The biopsy specimen taken from this lesion was reported as melanocarcinoma. The lesion is still present and the patient is alive, eight years later. It is my impression that a mistake was made by the pathologist.

DR. A. BENSON CANNON: I referred the child to a plastic surgeon to see whether an operation could be performed that would improve the appearance of the boy's face. The surgeon recommended that removal of the nevus followed by a skin graft would be the proper procedure and suggested that the patient be brought back the next summer to have the work done.

**Hydrocystoma** Presented by DR ANTHONY C CIPOLLARO

A S., a woman aged 50, born in Italy, stated that about one year ago she noticed a small lesion at the outer canthus of the left eye. This lesion has grown gradually. She has done nothing special about it.

The patient now presents a lesion which is about the size of a split pea, is translucent and is extremely tense. It appears to be filled with a clear fluid, possibly sweat, and causes the skin to be under great tension. The skin of the cyst wall shows several telangiectatic vessels. There are no inflammatory reactions, and the patient stated that there has never been any inflammation in or about the lesion.

## DISCUSSION

DR FRANK C COMBES: This is an unusual case, and I agree with the diagnosis. I think that I saw a similar case once, years ago.

DR HOWARD FOX: I agree with the diagnosis. This is a rare disease, said to occur in people exposed to heat, as in housewives. It is unusual to see only one lesion.

DR A BENSON CANNON: I think that one should rule out the possibility that this may be a cyst of the meibomian gland, inasmuch as it involves the mucous surface of the lid as well as the adjoining skin.

DR EUGENE F TRAUB: While I believe that single lesions of hydrocystoma are not common, it is of interest that 2 patients with such lesions were recently shown at the New York Academy of Medicine and a patient with a single lesion was also seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. I mention this because in the first 2 instances the lesions were mistaken for some type of tumor, one having been thought to be a melanoma and the other being labeled hemangioendothelioma. It should be stressed that lesions of hydrocystoma do occur singly and that when they do they are not infrequently much larger lesions than when groups of multiple sweat cysts are found.

**Poikilodermatomyositis** Presented by DR GEORGE M LEWIS

D M., a white housewife aged 40, is presented from the New York Hospital. In March 1943 she first noticed a small red scaly patch in the left axilla. This increased in size, and the right axilla subsequently became affected, followed by involvement of the arms, the dorsa of the hands and the pubic region. Erythema of the face and swelling of the eyelids were first noted only a few months ago. In July 1943 weakness of the legs developed, and it has been a troublesome symptom ever since. The arms have also shown this symptom. Other symptoms and signs which have developed include nocturnal fever, increased perspiration, pruritus of many cutaneous areas and tenderness over the distal phalanges. Recently there has been restriction of movement of the arms because of the development of fissures in the axillae. Erythematous areas were noted on the face, including the eyelids, on the dorsa of the fingers and over the axillae. Telangiectatic macular and slightly elevated areas were present on the chest and, to a large degree, on the legs. The deltoid muscles showed some irregular doughy masses. A biopsy of a specimen from the left deltoid muscle showed considerable degeneration and an inflammatory perivascular exudate. The blood count showed 5,200 white cells, the other elements of the blood being normal.

The Mazzini test was negative and the urine normal. Both the ascorbic acid and the glucose tolerance tests showed lowered values. All other routine tests showed normal results.

## DISCUSSION

DR ANTHONY C CIPOLLARO: I am much interested in this disease because scleroderma, poikiloderma, dermatomyositis and Raynaud's disease are seldom clear-cut. In other words, features of all these diseases may be seen in any one of them.

Even though the clinical manifestations vary, I believe that the underlying pathologic changes are common to all of them. Not all patients respond to treatment, but some do improve under the influence of vasodilators.

DR MAURICE J COSTELLO I wonder what relationship this eruption has to lupus erythematosus, since all the lesions are on the exposed portions of the shoulders and the V of the chest.

DR GERALD F MACHACEK As far as I can make out, evaluation of cases of this group, including poikilodermatomyositis, scleroderma and dermatomyositis, is difficult, and to separate particular cases and classify them is sometimes almost impossible. I do not know why one should call this poikilodermatomyositis and not consider disseminated lupus erythematosus.

DR GEORGE M LEWIS The cases of dermatomyositis seen at the New York Hospital have varied considerably in their clinical features. This woman shows the features of weakness of muscle groups, together with cutaneous changes. Most of the changes in the skin are more suggestive of poikiloderma than of lupus erythematosus, and there are also sclerodermatous changes in some areas. I believe that dermatomyositis is a well defined entity which can be distinguished from lupus erythematosus, poikiloderma and scleroderma, although in this case all three diagnoses might be considered.

#### A Case for Diagnosis (Fibrosarcoma?) Presented by DR MAURICE J COSTELLO

A B, a woman aged 58, was first seen by me on Nov 2, 1944. She stated that she had a tumor removed from her back five years ago. In September 1943, a mass was excised from her right groin, which consisted of two encapsulated nodules irregularly oval in shape, one measuring 2 by 1.5 cm and the other about 9 by 4 cm. On section they were yellowish and semitranslucent and were rubbery in consistency. Smaller nodules were removed from the buttocks at that time. The microscopic diagnosis was neurofibroma. On November 10, an irregular nodule, measuring 4 by 3 cm, was removed from the right thigh. On section it was hard, glistening white in some areas and flesh colored in others, presenting a rather homogeneous appearance. The microscopic report at that time was as follows:

"This is a tumefaction which varies in its cellularity, in some areas it is highly cellular, while in others it shows a considerable amount of collagen. The majority of cells are fibrous connective tissue cells, some of which are spindle shaped and others of which are polygonal. They are unequal in size and shape, differ in their staining qualities, have hyperchromatic nuclei and show a moderate number of mitotic figures. The microscopic diagnosis is fibrosarcoma of the thigh."

At the present time, the patient presents a number of pea-sized to half-dime-sized discrete, flat, shotty, firm lesions on the right buttock, the right hip region, the right side of the abdomen and the right inguinal area. Some of these lesions are invisible and can be appreciated only on palpation. The patient states that the pruritus is intense, although none of the signs of chronic itching are present. Recently, the patient has complained of severe pain in the right upper extremity. She has not lost weight or strength. A slide of the section, removed in September 1943, is available for study.

#### DISCUSSION

DR EUGENE F TRAUB If roentgen ray therapy has not been tried in large doses, I should suggest trying it. Some of the lesions looked almost like lymphoblastoma, in other words, like a lymphosarcomatous infiltration of the skin rather than neuromatous or fibromatous infiltration.

DR GEORGE C ANDREWS Roentgenologic treatment should be tried in this case. The eruption is a little unusual in appearance. Most cutaneous fibrosarcomas are not plaque-like inflammatory indurations of the skin, such as these are, but are rather elevated papules and nodules that are not so inflammatory.

DR GERALD F MACHACEK This should be considered a rare lesion. It is not often that one sees fibrosarcoma of the skin. In my opinion, the histologic changes are those of sarcoma rather than those of one of the lymphoblastic infiltrations, although I have seen not dissimilar cases of lymphosarcoma.

DR MAURICE J COSTELLO I also think that this eruption has the features of lymphoblastoma. These lesions are extremely pruritic, they have already responded to roentgen rays, and the itching has been relieved by this form of therapy.

**Lichen Nitidus** Presented by DR MAURICE J COSTELLO

R C, a girl aged 7, has had a generalized eruption for the past year, including the face, especially around the commissures of the mouth, the torso, where it is profuse over the chest, and the flexor aspects of the upper and lower extremities. The eruption consists of numerous pinpoint, flat-topped, shiny, polygonal, closely aggregated papules in patches varying in size from that of a nickel to that of a palm. When the fingers are passed over the areas, there is a nutmeg grater sensation. There is some lichenification of the patches on the flexor surfaces of the wrists due to scratching. Treatment has consisted of application of a keratolytic lotion and administration of large doses of vitamins A and D.

#### DISCUSSION

DR GERALD F MACHACEK The grouping of the lesions suggests lichen scrofulosorum rather than lichen nitidus, but the patient seems to be in excellent physical condition. Pityriasis rubra pilaris is a possibility to be considered.

DR GEORGE C ANDREWS As several others have suggested, I think that it probably is just mild early pityriasis rubra pilaris.

DR EUGENE F TRAUB It was also my impression that this might be a case of early pityriasis rubra pilaris in which all the characteristic features had not yet had time to develop.

DR HOWARD FOX I cannot agree with the diagnosis as presented. The lesions are not bright and shiny, as the name implies, and they are certainly scaly. I have never seen a case of lichen nitidus so profuse as this. There are not enough typical lesions to warrant the diagnosis of pityriasis rubra pilaris, there are no thickening and no lesions on the backs of the fingers or in the scalp. I think that this disease might yield to vitamin A in large doses. This also helps in many cases of pityriasis rubra pilaris (a disease which may be in the same category).

DR PAUL E BECHET In my opinion, the clinical evidence does not warrant a diagnosis of lichen nitidus. There is too much hyperkeratosis, and the lesions are too acuminate. The characteristic shiny, pinhead-sized, almost flesh-colored, discrete papules of lichen nitidus are conspicuous by their absence.

DR FRED WISE I cannot offer a diagnosis, but some of the lesions, particularly those on the outer side of the thigh, near the groin, can be taken for lichen nitidus. They are definitely shiny and elevated. But whether the whole picture is that of lichen nitidus I am unable to say. I should rule out pityriasis rubra pilaris for many reasons, because this eruption, to the extent seen here, would have a peculiar orange-yellow color, and no such color can be seen here. I should like to see a report of a biopsy.

DR MAURICE J COSTELLO From the clinical point of view, I should not favor pityriasis rubra pilaris. In addition to the points made by Dr Wise, there is no sharp demarcation of the eruption, as is found in that dermatosis. I based my diagnosis on the original lesions, which were flat, shiny and discrete.

**Recurring Stomatitis** Presented by DR HOWARD FOX

I C, a Jewish salesman aged 42, has suffered from an eruption of the tongue and soft palate for the past year and a half. Until ten days ago the disease had been confined to the mouth. The eruption consists of small, white patches on the

right side and tip of the tongue, which have been present without remission since the onset. The patient states that one or two lesions appear nearly every day and last only a day or two. He has not noticed any vesicles or bullae on the tongue. The eruption does not cause any soreness and does not interfere with eating or drinking. About ten days ago, he noticed an eruption on the lips, which he considered to be "cold sores."

Three days ago, when first seen by me, there was a bean-sized white patch on the right side of the tongue, which looked as if silver nitrate had been applied. Today this lesion is red but is neither painful nor tender. The soft palate shows a stippled, nontender and erythematous eruption. On the lips are crusts which suggest erythema bullosum, and on the chin there are a few red scaly macules.

The patient is in good general health but is overweight. He has lost no weight since the onset of the disease. He was born in the United States, where he has always lived. He was formerly a heavy smoker of cigars but of late has smoked moderately. He does not take alcoholic drinks to excess and has used the same dentifrice for years. He does not suffer from indigestion.

He has seen many physicians, some of whom have treated him for vitamin deficiency. He has had large doses of riboflavin and ascorbic acid, without any improvement. Just before the eruption appeared, he was given injections of poison ivy extract for prophylactic treatment. He is not accustomed to taking any drugs and has never been treated with either sulfonamide compounds or penicillin.

The blood count and urine were normal, and the Wassermann reaction of the blood was negative. Examination for Vincent's organisms gave negative results on two occasions.

#### DISCUSSION

DR MAURICE J COSTELLO I think that this patient has erythema multiforme of the bullous type.

DR FRED WISE Pemphigus must be suspected in this case. If this is a true virus disease, it might be desirable to give this man a series of cowpox inoculations.

DR ANTHONY CIPOLLARO I think that this patient has pemphigus, and I agree that the therapeutic suggestion made by Dr Wise should be tried. However, if the eruption should persist then I should advise intravenous injections of sodium nitrite given three times a week.

DR FRANK C COMBES I disagree with Dr Wise. I cannot conceive of lesions appearing and disappearing at such short intervals. Also, it does not look like pemphigus. It is too clean. I should think of erythema bullosum. It might respond to smallpox vaccination. I am now treating 1 patient with an eruption confined to the lips. She was considerably improved by vaccination during a previous attack and has stayed free of it for six months. She now wants to have additional vaccinations. I am not ready to say definitely that the vaccination is responsible for her freedom from recurrence.

DR EUGENE F TRAUB In reference to smallpox vaccination, I should like to ask the persons who recommend this whether the results of the therapy are equally efficient if there is no reaction, or take. It has been my impression that if one does not get a take one need not expect any results from this type of therapy. I have discussed this with a number of other dermatologists, who are of the same opinion.

DR HOWARD FOX I felt that nearly every one who saw this man today would say that he was suffering from pemphigus. I am doubtful about this diagnosis as I have never seen a case of pemphigus or of bullous erythema multiforme in the mouth that did not cause a good deal of pain, which interfered with eating and resulted in a loss of weight.

#### A Case for Diagnosis (Microaerophilic Ulcer?) Presented by DR A BENSON CANNON

B B, a man aged 42, has had ulcers for the past one and a half years. The process began as a "boil" on the right leg and broke down and extended. The

original lesion partly healed, but new lesions continued to appear and spread from the old borders. The patient's general health has always been excellent. There are no contributory data in the past history.

A study of the patient at the Morristown (N. J.) Memorial Hospital, before he came to the Vanderbilt Clinic, showed the following. Urine and complete blood count were normal. Blood cultures showed no growth. Cultures of material from the ulcers on the leg showed staphylococci and gram-negative bacilli. A biopsy specimen was reported as inflammatory tissue. The Kahn test elicited a negative reaction.

The patient received penicillin ointment locally and intramuscular injections totaling 550,000 units in ten days (5,000 units every four hours), he also received potassium iodide, 10 drops three times a day, gentian violet medicinal, liquid petrolatum, and zinc oxide.

Since admission to the Presbyterian Hospital, tests have elicited the following results. The sedimentation rate, urine and complete blood count were essentially normal. The serum sugar level was 73 mg per hundred cubic centimeters, the Wassermann reaction of the blood was negative. The blood showed a faint trace of bromide, and the biopsy specimen was reported as showing inflammatory tissue. Cultures of the ulcers were negative for fungi and amebas and positive for hemolytic streptococci, *Staphylococcus albus* and hemolytic *Staphylococcus aureus*. All cultures showed *Bacillus coli*, and anaerobic cultures were negative. Smears showed gram-positive cocci and gram-negative bacilli.

The microaerophilic culture has not yet been reported on.

Therapy at the present time consists of injections of penicillin intramuscularly, 25,000 units every three hours, local applications of one-half strength solution of hydrogen peroxide (U. S. P.) by irrigation twice a day, potassium permanganate wet dressings during the day (1:1,800 potassium permanganate) and boric acid ointment dressings at night.

#### DISCUSSION

DR ANTHONY CIPOLLARO. The peculiarity of these ulcerations is that the ulcer does not affect a previously affected area, in other words, it affects normal skin and always stops at the place where an ulcer has previously attacked. One of my patients pointed this out to me, stating that the ulcer always extended away from the scar. It invades new skin but never scar tissues. In this case too, the man has lesions on the leg along the periphery of the scar rather than on the scar itself.

DR PAUL E. BECHET. It is difficult in some of these patients to eliminate the possibility of an artefact, at least as the first contributing etiologic factor. When this factor has been definitely eliminated, I have found that constitutional treatment of a supportive nature, such as rest, sunshine or generalized exposure to ultraviolet rays, combined with vitamin therapy and intravenous injections of ferric cacodylate, are of importance equal to, if not greater than, local treatment.

DR ANTHONY CIPOLLARO. For the present I should accept this diagnosis because I cannot offer any other, but these are gangrenous lesions which are not always due to the microaerophilic streptococci. I believe that there are other causes, which as yet have not been determined. I feel that there is always some constitutional deficiency in these cases. I had success in treating 1 woman patient with this disease with injections of liver and sulfathiazole by mouth. Even though there are no clinical evidences of this disease, I am continuing to give an iron preparation by mouth and injections of liver twice a month. I think that this is good prophylactic therapy.

DR FRANK C. COMBES. All the characteristics shown by these ulcers correspond closely to the disease described in North Australia as pyoderma ulcerosum tropicum. What struck me particularly were the elevated, thickened, rolled borders and the lack of involvement of previously involved tissues, the painful nature of the ulcers earlier and their indolent nature now. These ulcers have been described as being exceptionally severe and protracted. The causative organisms are classified as



group A hemolytic streptococci and *Staphylococcus aureus*. Treatment has been with sulfapyridine ointment, 3 per cent, locally and large doses of vitamin C internally.

DR GEORGE M LEWIS I agree that the patient exhibits a gangrenous ecthymatous infection.

DR GEORGE C ANDREWS Paracoccidioidomycosis resembles coccidioidal granuloma, and I believe that Dr Cannon will report that the cultures and smears in this case were negative. Pyogenic gangrene does not always occur in debilitated persons. The last patient in this category that I treated was a student from Columbia University who rowed in the varsity crew and was in perfect physical condition. He was cured by local treatment. Sulfadiazine internally did not do him any good, but cleaning the ulcers out every day and using zinc peroxide dressings were effective.

DR GERALD F MACHACEK Histologically, no etiologic agent was disclosed, there was no fungus or ameba. Spontaneous ulcerations of the scrotum, which are idiopathic, have been described by urologists and others, usually in association with enteritis or abdominal operation. The histologic study did not elucidate this case.

DR MAURICE J COSTELLO I agree with the diagnosis. This patient has the microaerophilic hemolytic streptococcal ulcers described by Meleney. I have had 3 of these cases, and in Meleney's work at that time he presented many photographs with exactly the picture this patient presents. It is a difficult disease to treat successfully. If the lesion, for instance, is on the abdomen, it must be removed surgically with an ample border and the wound then packed with zinc peroxide cream and kept wet all the time, covered with petrolatum gauze. Best results are obtained when sulfanilamide tablets are combined with this treatment.

#### **Epidermodysplasia Verruciformis** Presented by DR FRANK C COMBES

J L, a boy aged 16, presented an eruption confined to the trunk and upper extremities, which appeared approximately a year after birth. It has varied little since then, other than becoming slightly erythematous and itching in hot weather. The distribution is bilaterally symmetric and is especially profuse over the anterior part of the trunk, although on close inspection it is almost as extensive on the back, but the individual lesions there are not so protrusive and prominent. No lesions are present on the face, palms or soles, although several appear on the backs of both hands. The individual verruca is a small, mamillated, sessile or obtuse papule, 2 to 5 mm in diameter, and some of them coalesce to form small plaques, 1 to 2 cm in width. In general the outline of these lesions is irregular or polygonal. On palpation they are rough and dry, and they are grayish brown, although some are slightly reddish. The intervening skin is normal. The number of lesions present approximate about twenty to each square inch (65 sq cm) of skin on the trunk.

Subjective symptoms are absent, although the patient says that the eruption irritates him somewhat at night and in hot weather it is red and itches. Physical examination otherwise gave normal results.

Histologic examination of a section of skin, which included one of the lesions on the left side of the chest of the patient, showed, under low magnification, that the epidermis was unusual in that there were many areas in which it was thin and other areas in which there was a modified hyperplasia of the prickle cells. In some locations there was a definite infolding of the epidermis, as is usually seen in verruca vulgaris. In these places there was acanthosis and the basal cells were numerically increased, separated and arranged in nests. Some of the nests were lined with keratin. In some areas the prickle cells appeared normal, and in others there was a tendency toward vacuolation around the nuclei. The affected cells were larger than normal and showed definite signs of degeneration by a lack of distinct staining, a loss of nuclei and the formation of small cavities. Intercellular bridges between these dyskeratotic cells could not be discerned. A hyperkeratotic scale

surmounted the lesions, but there was no parakeratosis. The rete pegs were broadened and in places fused. There was a mild round cell infiltration in the papillary layer of the corium.

## DISCUSSION

DR HOWARD FOX. I believe that this is the second case to be presented before the society. I agree with the diagnosis.

DR GERALD F. MACHACEK. I agree with the diagnosis. Some lesions may ultimately go on to malignant degeneration. One case, in which I had an opportunity to examine numerous sections, showed degeneration which histologically was Bowen's disease.

DR FRED WISE. I agree with the diagnosis. I have seen 3 cases. 1 case was shown by Sullivan of Baltimore, and 2 cases were seen here. The patient in 1 of the cases on which I reported at first had no sign of active epithelioma anywhere on the body, and two years later he had an epithelioma on the forehead, which Dr Machacek described as Bowen's disease.

DR A. BENSON CANNON. I think that Dr Combes should be complimented on making a clinical diagnosis before having the pathologic report.

## Basal Cell Epithelioma Presented by DR ANTHONY C. CIPOLLARO

J. E., a fireman aged 38, was first seen by me on Sept. 29, 1944, because of a lesion on the left lower eyelid, of four years' duration. The patient stated that he first noticed a spot on the edge of the left lower eyelid near the inner canthus about four years ago. He did not do anything about it, although he had shown it to physicians. About one and a half years ago a general practitioner burnt it out, and it promptly recurred. During the past several months it had been spreading rapidly, and the patient consulted several physicians about it but nothing was done.

On examination there was a lesion affecting the inner half of the left lower eyelid. There were two different clinical appearances to the lesion. The outer half was ulcerated, with a definite pearly border. A portion of the border, including the ulcer, invaded the margin of the lid and the conjunctiva for a distance of about 2 mm. Nearer to the nose there was an elevated, pea-sized, firm tumor, with telangiectatic vessels overlying it. One lesion encroached on the other.

On October 2, the skin about the epithelioma was anesthetized with procaine hydrochloride and the conjunctiva was anesthetized with 1 per cent phenacaine hydrochloride solution. The lesion was thoroughly curetted and desiccated under magnification, and a boric acid ointment dressing was applied. The patient was then given four roentgen ray treatments, each consisting of two erythema doses (600 r) of unfiltered roentgen rays. The treatments were given on October 5, 11 and 18 and on November 10. In order to be certain that the tumor bed was uniformly irradiated, additional radiation was applied, 45 mg of radium filtered through 0.5 mm of platinum being used and kept in contact for thirty minutes. These treatments were given on October 18 and 25. The eyeball was protected with a brass eye shield.

When the patient was last seen, on November 29, the lesion appeared to be completely healed and there was roentgen erythema about the tumor bed.

Histologic examination showed "basal cell epithelioma en masse."

## DISCUSSION

DR FRANK C. COMBES. This is a beautiful result and probably will be permanent.

DR EUGENE F. TRAUB. The result in this case is excellent, and from the present examination it seems reasonably certain that it will remain so. It has been my opinion that the treatment of choice for epitheliomas about the eyelids is a

combination of desiccation, curettement and radiation, as was carried out in the present case

DR GEORGE C ANDREWS This is a beautiful result

DR ANTHONY C CIPOLLARO The results of treatment with a combination of electrosurgery and radiation of epitheliomas affecting the margins of the eyelids have been satisfactory in my experience I do not believe that extensive surgical treatment, including enucleation of the eye, is necessary in the management of lesions of this type

### Acrodermatitis Chronica Atrophicans with Angiosarcomas Presented by DR FRED WISE

J G, a woman aged 60, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Nov 21, 1944, presenting growths on the right ankle and foot, of two years' duration, and a "condition of redness of the skin," of twenty years' duration She complains of itching of the right leg but not of the foot The growths on the foot are neither painful nor tender The patient is otherwise in good health

A pea-sized growth first appeared on the outer side of the right ankle about three years ago This was destroyed by an electric needle Two new lesions appeared about two months ago

There are about one and a half dozen growths, discrete, purplish red in color and varying in size from that of a match head to that of a large pea They are palpable and not tender Most of the lesions are concentrated on the inner and under surface of the distal half of the right foot, where they are closely grouped, rounded, moderately infiltrated and covered by heavy crusting Pea-sized to bean-sized nodes are palpable in the left groin The patient has acrodermatitis chronica atrophicans on both lower limbs and enlarged varicosities, most evident on the right leg

Histologic examination of one of the lesions showed the following findings "The epidermis is moderately irregularly acanthotic except for its central portion, where it is thinned, with obliteration of the rete pegs and corresponding papillary bodies Underneath the latter there is a mass composed of spindle cells Scattered throughout this mass are many small, thin-walled blood vessels Similar but less well defined masses are noted in the deeper portions of the corium The vessels throughout the section are dilated, and some of them are surrounded by a mild cellular infiltration composed of small round cells The Perl reaction was negative The diagnosis was angiosarcoma and acrodermatitis"

DR HOWARD FOX It is unusual to see malignant changes in cases of acrodermatitis chronica atrophicans

DR GEORGE M LEWIS Martin has described malignant degeneration in acrodermatitis Dermatologists seldom see this complication, but apparently the men who specialize in cancer observe it more frequently

DR EUGENE F TRAUB I should like to ask Dr Wise if the sarcoma developed on the plantar surface of the foot on the instep or in the area of the acrodermatitis, as the lesion seems to be such an extensive one at the present time that it is difficult to determine the point of origin of the sarcoma The little experience I have had with the treatment of sarcomas in this location and depending, of course, also on their degree of malignancy is that they are hard to eradicate In this case, with the widespread area of involvement, if anything is to be attempted locally it may be necessary to do an amputation of the foot to effect a cure

DR GEORGE C ANDREWS Dr George Pack reported 3 or 4 cases of this disease complicated by epithelioma and considers it to be a precancerous dermatosis

DR GERALD F MACHACEK Histologically, this appears to be a sarcomatous process In any event it is important to differentiate between that and Kaposi's sarcoma When one considers a sarcomatous process pure and simple an amputa-

tion may be in order, but if it is Kaposi's sarcoma one would be loath to recommend such a course, as the latter is a systemic involvement

DR FRED WISE In answer to Dr Traub's question, areas of edema accompanying this growth appeared in the previously affected areas, and with respect to treatment, in view of the patient's age and general condition, it was decided, on consultation at the New York Post-Graduate Medical School and Hospital, that deep roentgen ray therapy should be tried before the more radical surgical treatment is resorted to

**A Case for Diagnosis (Dermatitis Medicamentosa)** Presented by Dr EUGENE F TRAUB

E S, a woman aged 56, was first seen at the Skin and Cancer Unit of the Post-Graduate Medical School and Hospital about November 20. She stated that she had been treated for a ragweed allergy and on November 8 had received 10 units of ragweed extract. Two days following the injection a mild eruption developed on her face, right arm, forearm and hand. On November 15 she was given an injection of 20 units of ragweed extract, directly after this the right hand swelled and the eruption became much worse. The only other history of ingested medicine was that of expectorant mixture, which was taken without codeine. This, however, was discontinued two days before she received the first injection of ragweed extract and, therefore, four days before an eruption appeared. At the present time she presents patches of erythema scattered over the right hand, forearm and arm, with somewhat elevated borders and polycyclic outlines. The hand and forearm are greatly swollen. Her face shows a number of annular lesions, particularly a large one on the right cheek and in the temple area, which had a hard elevated border and strongly suggested either a sarcoid or a granuloma annulare. There were a similar, but smaller annular lesion on the bridge of the nose and erythematous patches scattered over the forehead and face. The patient was given a soothing lotion and mild zinc oxide ointment locally and has improved under this regimen.

Since the patient was presented, she has been given the expectorant mixture to take for two days in rather liberal doses, without a flare-up of her eruption. Furthermore, all the lesions practically disappeared within two or three weeks after presentation, so that there seems little question but that this was an eruption produced by the injections of the ragweed extract.

DISCUSSION

DR GEORGE M LEWIS I agree that the condition is dermatitis medicamentosa. This is not the common cutaneous response to ragweed extract. The cause might be some drug, the ingestion of which was not elicited in the history. If not, perhaps some of the ingredients of the expectorant mixture which she took are responsible.

DR RAY H RULISON I agree with the diagnosis presented. I think that the eruption is a reaction to ragweed extract.

DR HOWARD FOX I agree with the diagnosis as presented. The eruption appeared two days after the first injection, and a week following the second injection the patient got worse.

DR FRANK C COMBES I agree with Dr Traub.

DR A BENSON CANNON The bilateral, symmetric, circinate, nodular red lesions on this patient's cheeks are strikingly like sarcoid or lupus erythematosus, and I suggest that a biopsy be made.

DR FRED WISE I am in accord with Dr Cannon. I question whether this is due to ragweed extract.

DR GERALD F MACHACEK Only recently we had a similar case, that of a patient with an eruptive flare-up following the ingestion of some medicament. On histologic examination the lesion proved to be a lupus erythematosus.

DR GEORGE C ANDREWS I did not examine the patient carefully, but if this is a case of ragweed dermatitis occurring after injections to immunize her against ragweed then there is an extract counterpart of this case reported in the *Journal of Allergy* for May 1944 by R A Cooke, of Roosevelt Hospital, who stated that three times after injections of ragweed extract lesions broke out on the face and arms

DR EUGENE F TRAUB The duration of the eruption in this patient was three weeks The history is definite that the eruption followed within two days after her first injection of ragweed extract and that it again flared up, a week later, after her second injection No further injections were given, and the eruption began to disappear, with practically no treatment except the soothing local application The history, therefore, seems definitely to tie the process in with the injection of ragweed extract, particularly since the only other medicine was discontinued two days before the first injection was given Before this history was obtained, the eruption on her face suggested the possibility of sarcoid, lupus erythematosus or even granuloma annulare

### Tertiary Syphilis Presented by DR ANTHONY C CIPOLLARO

I E, a 67 year old white woman born in the United States, first attended the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Sept 8, 1943 She gave a history of having had lesions on her face on and off for thirty years, and she was told that she had tuberculosis of the skin During all this time she was treated only with ointments Ulcers would form and close up, and others would form Three months prior to her visit to the clinic she had painful ulcerations at the junction of the nose and upper lip, which nothing seemed to relieve

On examination there were many scars of different sizes and different forms scattered over her face There were some nodules and also some active ulcerations The largest ulcer was at the junction of the nose and upper lip This ulcer was painful and interfered with eating, talking and other movements of the mouth The ulcer was sharply demarcated and appeared punched out

The right lower eyelid showed a definite ectropion, and at the outer edge of the right upper eyelid there was a small mass, which had been present for years The surface appeared to be verrucous, but there was no definite ulceration or infiltration The nature of this lesion has never been determined The patient was examined in the eye clinic but an operation for this lesion was not advised

The syphilitic history is negative except for the fact that she has never been pregnant, has never had a blood Wassermann test and has never been treated for syphilis

Physical examination was entirely normal The Wassermann reaction of the blood was 4 plus An examination of the spinal fluid was not made The blood count and urine were essentially normal A biopsy specimen was diagnosed as "granulation tissue, there was no evidence of tuberculosis"

Mixed treatment was prescribed, and the active lesions promptly responded

The patient is presented for opinions regarding the nature of the lesion on the forehead

### DISCUSSION

DR PAUL E BECHET I agree with the diagnosis, the peripheral extension and healing center are characteristic Malignant growths are occasionally seen superimposed on old syphilitic lesions but, of course, not to the extent of those occurring in lupus vulgaris

DR FRANK C COMBES If anybody had asked me if it were possible for any one to be in New York for thirty years and, having syphilis, not to have had a Wassermann test made, I should have said it was impossible As to the lesion on the lid, it is difficult to say clinically what it is It may be a pyogenic granuloma It is not malignant

DR HOWARD FOX There is no question about the scars being due to syphilis, though it is somewhat unusual to see such decided symmetry in syphilitic scars

DR EUGENE F TRAUB I have a definite idea about the lesion on the eyelid. This patient evidently had a rather destructive lesion at one time on that lid, with a resulting contracting scar, which produced an extensive ectropion. If one observes the lid carefully at the present time, it is easy to see that what appears to be a tumor is simply the everted lid showing the red granulating surface of the conjunctiva. The eyelashes at the margin of the lid are turned back and involved in the process. I do not believe, therefore, that she has a malignant lesion or tumor of any type but simply has a red, raw, granulating surface representing conjunctiva in a severe case of ectropion.

DR GEORGE C ANDREWS I do not think that this lesion is a tumor. My impression is that it is a chronic inflammatory condition.

DR JOHN C GRAHAM My feeling was that it was not malignant. I thought that Dr Traub's explanation was valid.

DR MAURICE J COSTELLO I think that this is granulation tissue. If it were epithelioma, I wonder where one would begin and where one would end with surgical treatment. The whole lid is involved.

DR A BENSON CANNON We have 3 cases of most extensive scarring from gumma at the Vanderbilt Clinic. Each case presents much more destruction than is found in this patient. Our 3 patients had had lesions from fifteen to thirty years without ever having had serologic examinations made. The patients showed advanced destruction not only of the soft parts and bones of the face, skull, upper extremities and chest but, in 1 case, of both legs from the knees down.

DR ANTHONY CIPOLLARO It is, of course, unusual to see a patient with syphilis for thirty years who has not had a Wassermann test made. The tumor on the eyelid was studied carefully, I do not know its nature. I do not believe that this is a cancerous tumor. However, I see no harm in performing a biopsy.

#### **A Case for Diagnosis (Leukemia Cutis?) Presented by DR A BENSON CANNON**

N K, a white Jewish postal clerk aged 37, first presented himself at the Vanderbilt Clinic on July 7, 1944, complaining of an eruption on the forehead, eyebrows, cheeks, neck, left leg and buttocks, of eighteen years' duration. He has had previous hospital study, including biopsies, but has had no relief of his lesions from any treatment given to him. He has also received treatment for duodenal ulcer. The patient states that he is better in summer, as the skin is not so red then.

The patient appears to be in good health generally, except for the cutaneous eruption. There is a diffuse erythema of a pinkish character on the forehead, eyebrows, cheeks and neck. Discrete, waxy, cystlike, split pea-sized, pale, erythematous papules are distinct on the forehead. These vary slightly in size. Similar elements are found on the right buttock. None of the lesions are horny or follicular. There is atrophy in some places on the forehead. The hair is sparse on the eyebrows and sparser on the left and down over the cheeks and sides of the neck.

The blood count showed a hemoglobin content of 13.6 Gm, 4,750,000 red blood cells, and 7,800 white blood cells, with polymorphonuclear leukocytes 62 per cent and lymphocytes 28 per cent. The Wassermann reaction of the blood was negative. The basal metabolic rate was minus 16 per cent. Roentgenograms of the sinuses showed a clouding of the left maxillary sinus, suggesting sinusitis, and hypertrophy of the intranasal structures.

Histologic examination of a nodule removed from the neck showed infiltration of the mononuclear cells. There was no evidence of collagenous degeneration. Some elastosis was present, and tiny, keratin-filled cystic comedos were seen. The diagnosis was leukemia cutis (?).

## DISCUSSION

DR GERALD F MACHACEK Perhaps I should revise my diagnosis somewhat. I still think that the lesion is an infiltration of lymphoid cells, but I should call it lymphadenosis rather than a leukemic infiltration.

DR GEORGE C ANDREWS These are small, infiltrated papules in the skin that look like lymphadenosis or solitary lymphadenoma or possibly leukemia, although the lesions are a little soft. I believe that Dr Machacek's statement is probably correct.

DR EUGENE F TRAUB As far as the term "ulerythema ophryogenes" is concerned, I always thought that it was a scarring type of folliculitis limited to the eyebrows. Certainly the papular eruption scattered on the face would not conform with such a conception, and if the histologic structure, as Dr Machacek suggested, is that of leukemia cutis I believe that this would be a much more likely diagnosis and would account for all the changes seen at the present time in this patient.

DR GEORGE M LEWIS I think that the histologic interpretation is important. The clinical features are not typical for any disease with which I am acquainted.

DR FRANK C COMBES I agree with Dr Traub and with Dr Machacek's histologic interpretation.

DR HOWARD FOX I think that this is some type of lymphoblastoma.

DR A BENSON CANNON The eruption began in the eyebrows as a redness and scaliness that gradually spread over the forehead, cheeks and front of the scalp and resulted in the loss of eyebrows, in atrophic areas and in the formation of small, red, follicular papules. However, I was at a loss to explain the pea-sized nodules studded over the forehead, these making me suspect the possibility of leukemia. A biopsy on one of the nodules was reported as indicating leukemia.

#### Parapsoriasis Presented by DR MAURICE J COSTELLO

R A, a 45 year old Italian man, is presented from St Clare's Hospital outpatient department. He was first seen by me in the middle of October 1944. He stated that he was a bricklayer's helper and that he was under the impression that the eruption, which had been present since the beginning of October 1944, was due to his occupation. He was sent to me by his employer for a decision on the question.

He presented a generalized symmetric nonpruritic eruption, consisting of lentil-sized maculopapules profusely distributed over the torso and the extremities. Some of the lesions were covered with a solid adherent scale. A number of these closely aggregated, salmon-colored lesions along the posterior axillary folds and the waistline were slightly depressed, suggesting atrophy. Less conspicuous lesions were seen on the head, face and genitals. A biopsy was taken from the left thoracic region and presented the following findings:

"While the entire picture simulates parapsoriasis, the presence of large cells would make one suspicious of mycosis fungoides. The vessels of the upper mid-cutis are dilated, and about them is a moderate focal cellular infiltration. The epidermis shows no acanthosis, but there is considerable edema of the lower border and some parakeratosis in areas. The cellular infiltration is composed of small, round cells, some plasma cells and epithelioid cells."

The Wassermann reaction of the blood was negative.

## DISCUSSION

DR GERALD F MACHACEK I am willing to accept this as parapsoriasis undergoing atrophy. This is a clinical interpretation. There is not much to be seen histologically.

DR GEORGE M LEWIS I think that this is a most unusual and interesting case. The lesions show no infiltration. The presence of atrophy is unusual, but the diagnosis seems correct.

DR HOWARD FOX The eruption looks more like parapsoriasis than anything else, although it is of rather short duration. However, I cannot account for the atrophy seen on the hip.

DR PAUL E BECHET I agree with the diagnosis The atrophic, sharply outlined patches are most unusual in parapsoriasis en plaque but are common in parapsoriasis varioliformis, for these reasons the latter diagnosis deserves consideration

DR A BENSON CANNON I agree with Dr Fox's remarks

DR FRED WISE The eruption might well be parapsoriasis, but further investigation is certainly indicated There are peculiar clinical manifestations in this case I wish to call attention to an article by Kreibich describing parapsoriasis atrophicans, with lesions much like this except that they were larger I mentioned that article in a publication and showed a picture of the patient taken from the article

DR MAURICE J COSTELLO From the clinical point of view, parapsoriasis was the only diagnosis I entertained I am at a loss to understand, however, why atrophic lesions should be present in guttate parapsoriasis, unless this patient has parapsoriasis atrophicans The biopsy was done on one of the papules, not on one of the atrophic lesions

### LOS ANGELES DERMATOLOGICAL SOCIETY

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*Dec 12, 1944*

#### A Case for Diagnosis (Tuberculosis Verrucosa Cutis?) Presented by DR A FLETCHER HALL

H L E is a single white man, aged 39 years, who has no known tuberculosis in his family He has always been in good health and has lived in southern California for the past three years He has always lived in the United States He denies any use of bromides

The present lesion started as a pimple on the back of the right thigh twenty years ago, while he was living in Detroit It has gradually increased in size to the present 18 by 30 cm oval lesion Its surface has always been scaly, and its margin has been prominent Treatment has consisted of local applications for ringworm The patient has not taken iodide and has had no roentgen ray treatment The lesion is painful at times and bleeds easily in the central part, and the borders occasionally produce a serous exudate, with crusting

The entire posterior surface of the right thigh, most of the lateral aspect and the lower medial aspect are covered with a large plaque, all edges of which are verrucous and bleed on curettage Many scales and crusts are present along the border, with rather flat, dull red infiltrations beneath The border is well defined Some discrete daughter lesions are nearby The central portion is relatively clear but studded with dull red, scaly infiltrations, there is no true scarring, but the healed areas appear somewhat atrophic There are no milium abscesses or other pustular elements

Direct microscopic examination of scrapings from the papillomatous scaly border showed neither hyphae nor spores Culture on Sabouraud's medium showed no growth in one week Eagle and Kline tests of the blood were negative The biopsy showed no organisms with acid-fast stain Hemotoxylin and eosin stain showed irregular acanthosis, with "pinching off" of islands of the corium, but no abscesses were present The corium showed granulomatous reaction with edema There were numerous Langhans' giant cells and epithelioid cells and much round cell infiltration No blastomycetes were seen

Treatment has been started by the local application of roentgen rays totaling 200 r to each of six nonoverlapping areas The patient is also taking increasing doses of potassium iodide by mouth



## DISCUSSION

DR NELSON PAUL ANDERSON I think that this is a hypertrophic and verrucous type of lupus vulgaris I cannot conceive any other type of granuloma that would give this picture and persist over a period of twenty years

DR SAMUEL AYRES JR It does not seem possible that anything but lupus vulgaris could last that long and give a picture of that sort I did not have a chance to see whether apple jelly nodules were present, but I expect that they were in the border A tuberculin test was not noted on the patient's record, such a test would be helpful

DR M E OBERMAYER I agree with Dr Ayres and Dr Anderson on the clinical diagnosis, but I cannot reconcile the presence of large vascular spaces and of polymorphonuclear leukocytes in the dermis in a case of lupus vulgaris

DR KENDAL FROST I favor a diagnosis of blastomycosis

DR PAUL D FOSTER I think that this is a typical case of blastomycosis

DR HAL E FREEMAN I think that it is most typical of lupus vulgaris and that there is also tuberculosis verrucosa cutis present

DR H C L LINDSAY Lupus vulgaris may be simulated by syphilis and vice versa, especially when it involves areas about the nose The lesion presented looks like lupus vulgaris Nevertheless, syphilis should be considered

DR J WALTER WILSON If one is searching for blastomycetes, serial sections on the biopsy specimen should be done The organisms may be found in only one or two sections I have seen 1 case in which one could find organisms in only one fifth of the sections

DR A FLETCHER HALL This man misrepresented the history at first When he was seen a week ago he stated that his cutaneous disease was of three years' duration, and the motive for making that statement seems to be that for three and one-half years he belonged to a contract medical group and he would be eligible for treatment by them if the onset appeared since he joined the group When I first saw him, last week, I thought that the eruption was blastomycosis, but careful direct microscopic examination failed to show any organisms The group that sent the patient to me reported finding "myceliums and spores" in profusion in scrapings from the lesion This is the second time I have seen a case presented as blastomycosis in which the physician said that he found "myceliums and spores" Tonight the patient admitted that it was twenty years since the onset It seems to me that there is not enough scarring for lupus vulgaris In fact, the scarring seems slight for blastomycosis or any other infection of that depth of involvement Acid-fast stains of tissue sections have revealed no bacilli, nor have any fungous elements been found No tuberculin test has been made

NOTE—At the next month's meeting, Dr Hall made the following report

Serial sections of the biopsy have not shown any acid-fast bacilli or blastomycetes A large amount of tissue excised from the border of the lesion was injected into a guinea pig three weeks ago, and the animal is still well Fungi in cultures which developed since the presentation one month ago have been identified by Dr O A Plunkett, professor of botany at the University of California Medical School at Los Angeles, as *Scopulariopsis* He believes that this is the cause of the present lesions Further injections into animals are planned Involution of organisms is progressing under the local use of fractional doses of roentgen rays and the taking of 70 drops of potassium iodide three times a day by mouth This would indicate a fungus as the causative agent

### Chronic Dermatophytosis of the Feet and Erythema Annulare of the Face and Neck Presented by DR KENNETH L STOUT and DR MAXIMILIAN E OBERMAYER

C F C is a white man aged 36 years He had a streptococcic type of sore throat five years ago, severe enough to keep him in bed for ten days There was

a spider bite of the left leg about three years ago, which kept him in bed for three days

About ten years ago he consulted a dermatologist for an eruption involving the feet, groins and right hand. He was told that his condition was due to "fungous infection." The lesions on the feet were white, macerated, exfoliating plaques, with infrequent vesiculation involving the toes and heels. This condition has been present intermittently for ten years. The lesions on the right hand are dry, eczematous, diffuse eruptions of the palmar and volar surfaces. Such lesions have been constantly present for over ten years. Vesiculation has occurred between the fingers. The nails of the right hand have been thickened and discolored. The left hand has remained clear for three years.

The lesions on the face, neck and ears were first observed fourteen months ago. Of particular concern was a ringed lesion 3 cm in diameter, with a papular, elevated margin situated on the right cheek. The patient also had a less distinct, similar lesion on the upper lip. The lesions on the face disappeared in three weeks. There was a recurrence four months later, when a circinate lesion appeared over the left side of the nose. Gradually it spread peripherally across the nose and onto the left cheek, healing centrally and maintaining a solid, palpable elevated border. The patient complained of itching in these areas, and he developed the habit of rubbing the areas, producing some scaling. A month later, several new annular and serpiginous lesions developed on the left side of the face. Ten weeks ago the lesions on the face were almost entirely cleared, but seven weeks ago new, similar lesions had developed over the left side of the face, the left ear and the left side of the neck. A biopsy performed at this time on the lesion on the neck showed follicular plugging, a rather narrow stratum mucosum with intracellular edema and an edematous corium. There was vascular dilatation and perivascular lymphocytic infiltration.

The patient is in excellent general health. His skin is tanned from outdoor life.

The feet have moderate plaques, and there is peeling between the toes and scaling on the heels. The right hand is lichenified, dry and eczematous. This dermatitis diffusely involves the palmar and extensor surfaces of the hands. There is mild hyperkeratosis of the palms. The nails are thickened and discolored. The left side of the face, the left side of the neck and the left ear have annular serpiginous papular lesions. There is mild desquamation.

The trichophytin reaction was strongly positive thirteen months ago. It was 7.5 cm in diameter in forty-eight hours. Scales from the toes had numerous fungous filaments.

All lesions were recalcitrant to treatments which included roentgen rays in fractional dosage, 2 per cent solution of iodine, ointment containing 6 per cent each of sulfur and salicylic acid, 2 per cent tar paste, 2 per cent ointment of ichthammol, a 2 per cent aqueous solution of gentian violet medicinal, arsenous acid (asiatic) pills and a course of thirteen weekly injections of 1:100 trichophytin and 1:30 oidiomycin.

#### DISCUSSION

DR SAMUEL AYRES JR. I think that the whole picture is consistent with infection by *Trichophyton purpureum*. I believe that organisms could be found in the serpiginous lesion on the neck. For some reason, in cases of this type, the lesions on the face and other portions of the glabrous skin are not difficult to get rid of. Half strength ointment of benzoic and salicylic acid or salicylic acid and sulfur ointment often takes care of them, but the ones on the hands and feet are difficult to treat. I do not know the explanation of the clearing up of some of the glabrous cutaneous lesions in contrast to the persistence of the lesions on the hands and feet.

DR A. FLETCHER HALL. I agree with Dr Ayres. I have a similar case. My patient is a man whose right hand, feet and right side of the face are involved. I have not been able to clear up the face any better than the feet and the hand.

I did not notice any notation of scrapings having been made from the neck, but I think that they should be made, and made repeatedly. In my case, I made them six times before I got a culture of *Trichophyton purpureum*, all I got on the first five were contaminants. I suggest further studies of the lesions on the neck as well as of those on the feet.

DR KENNETH STOUT The history and clinical description in the presentation of this case were based on observations made about two months ago, when the biopsy was made. I did not see the patient again until yesterday. There has been at least a 50 per cent improvement of the eczematous lesion on the right hand and almost complete disappearance of the lesions on the face and neck except for the scaling. During the last two months the patient has spent much less time in his swimming pool, which may account for the improvement. The case is presented to provoke discussion on the relationship of the lesions on the feet, hand and face. It is unfortunate that the lesions on the face and neck do not show up well today. When first observed, they were definitely papular and annular and without scales. Later, scales appeared, which I thought were due to rubbing by the patient. The first annular lesion on the nose disappeared spontaneously in three weeks. Annular and gyrate papular lesions have undergone remission and reappeared in the same areas. Because of this behavior, I regard it as a manifestation of erythema annulare centrifugum, which is rare on the face and which some men feel may be trichophytids. The Suttons mentioned having 3 cases of erythema annulare centrifugum associated with vesicular tinea of the feet.

DR M E OBERMAYER I disagree sharply with the suggestion that the dermatitis of the face and neck could be caused by a fungous infection. Fungi on the glabrous skin are demonstrated with comparative ease. The mere finding of fungi between the toes would not allow the interpretation of the whole dermatosis as a form of dermatomycosis. In my attempt to reconcile the lesions of the neck and face with those on the hands and feet, I considered the diagnosis of atypical psoriasis. The biopsy, however, proved that I was wrong.

#### Hodgkin's Disease Presented by DR HAL E FREEMAN

P H is a white man aged 62. In September 1943 he noticed a swelling in the left axillary region. Soon after, he noticed swellings in the groins. For seven months he has had recurrent crops of vesicles on the face and scalp, and there have been recurrent pustules on the forearms and a persistent dermatitis on his face. He is exposed to zinc chromate paint.

Much of the skin is lichenified and excoriated. There are grouped vesicles on the scalp and erythema of the face, especially around the mouth. There is a tumor in the left axillary region, which is about 3 cm in diameter. There are several similar, smaller lumps in the inguinal regions.

Examinations of the blood showed 13.7 Gm of hemoglobin per hundred cubic centimeters of blood. There were 3,310,000 erythrocytes and 25,200 leukocytes, of which 26 per cent were neutrophils, 60 per cent lymphocytes, 4 per cent large monocytes, 9 per cent eosinophils, and 1 per cent basophils. A patch test of zinc chromate was negative after forty-eight hours and again after seventy-two hours.

#### DISCUSSION

DR L F X WILHELM I agree with Dr Freeman, that it is probably a case of Hodgkin's disease. A gland should be removed for biopsy.

DR HAL E FREEMAN I have seen this patient over a long period without recognizing the disease. Finally it dawned on me that this was a man with a lymphatic enlargement, severe pruritus with excoriations and a recurrent herpetiform eruption and that it might be a lymphoblastoma. The blood picture fitted in and was consistent with a diagnosis of Hodgkin's disease.

**Folliculitis Ulerythematosa Reticulata** Presented by DR MOLLEURUS COUPERUS

D B is a white boy aged 6 years. The lesion on the right cheek started with small pustules which became crusted about two years ago. When the lesions cleared up, the present scars were found. A few months later a similar patch appeared on the scalp just above and anterior to the right ear. This lesion on the scalp was treated one year ago by a roentgenologist.

The patient has a half-dollar-sized lesion on the right cheek. It consists of a network of depressed areas 2 to 4 mm in diameter, irregular in outline, with abrupt borders. The epidermis at the base of the lesion is wrinkled and thin. There is a similar patch, slightly smaller, above and anterior to the right ear in the scalp. In addition, the latter lesion has areas of depigmentation and telangiectasia.

## DISCUSSION

DR MOLLEURUS COUPERUS: I thought that the case was particularly interesting because of the fact that the lesions were unilateral. In most of the cases described, the lesions have been bilateral. This patient has had the lesions only two years. Maybe in five years they will be bilateral.

**Localized Scleroderma, Results of Bismuth Therapy** Presented by DR CLEMENT E COUNTER

B S is a white boy aged 7 years. He is presented to demonstrate benefit from bismuth therapy.

The present eruption on the left cheek began about eighteen months ago. The first lesion was oval, about 2 cm in its longest diameter and slightly higher on the left cheek than the present pigmented patch. It was thickened and ivory colored but not raised from the general surface of the skin. Its extension toward the left ear as well as downward toward the chin developed the present lesion. Eleven months ago there was an ivory-colored, round, hard lesion, approximately 3 cm in diameter, located on the lower portion of the left cheek, just posterior to a line drawn perpendicular through the left oral commissure. There was a pigmented, less thickened patch continuous from this hard lesion backward to the lower portion of the left ear, which was extended onto the neck below the left ear. The diagnosis then was localized scleroderma.

There is an irregular brown-pigmented patch on the lower part of the left cheek, extending from the left side of the chin to the lower part of the left ear, which is not indurated. The former hard, ivory-colored, thick, round part in the anterior portion of the lesion has lost its hard character and is merged into the other part of the mottled pigmented lesion. The lower part of the left cheek is smaller than the corresponding part of the right.

Treatment has included twenty-two intramuscular injections of a bismuth preparation, 1 grain (0.06 Gm) each given between Feb 15 and Dec 7, 1944. Injections were approximately two weeks apart. A daily dose of 1 grain of thyroid has been taken by mouth for the same time.

## DISCUSSION

DR H C L LINDSAY: Induration which is present is not easy to detect. I have never seen a patient with pigmentation exactly like this. It looks much like chloasma. The diagnosis is correct.

DR SAMUEL AYRES JR: I should like to clarify the picture again by asking how long the process had existed before treatment was given and how rapid was response to the bismuth. As Dr Lindsay said, there seemed to be some slight residual thickening. I should appreciate more information on the treatment.

DR CLEMENT E COUNTER: This boy had had the eruption about six months when he was first examined. That was about seven months before treatments were

begun I presented him before this society eleven months ago, and Dr Nelson Paul Anderson suggested the bismuth therapy Improvement has begun The father was so enthusiastic about the treatment from the start that I had to be careful in evaluating results Any one can see the present improvement At first, the round, ivory-colored part became pigmented across the middle, and now the induration is gone so that one cannot identify where it was

DR SAMUEL AYRES JR What was the *modus operandi* of the bismuth?

DR CLEMENT E COUNTER It is an empiric idea as far as I am concerned Bismuth subsalicylate was injected intramuscularly

DR L F X WILHELM I think that Dr Stokes recommended bismuth hydroxide

DR A FLETCHER HALL It is noteworthy that one by one more diseases are being added to the formidable list that bismuth "cures"—syphilis, lichen planus, lupus erythematosus, warts, sore throats, vitiligo and Vincent's angina

#### Congenital Defect of Hair Presented by DR SAMUEL AYRES JR

J G is a white girl aged 10 years The condition has been present since birth and consists in the inability of the hair to grow beyond a few inches According to the mother, when the hair attains a length of about 2 or 3 inches (5 or 7.6 cm) it falls out, but new hair comes in to replace it

The hair on the scalp is abundant and of good quality, but it is relatively short It has an average length of 3 inches (7.6 cm) on the top of the head and can easily be pulled out The hair on the arms, legs and thighs and lower part of the back is perhaps somewhat heavier than normal, considering the age of the patient The skin is normal

The patient is presented for suggestions as to cause and treatment

#### DISCUSSION

DR KENNETH STOUT I wonder whether endocrine substances would be of any help I doubt it I think that it would be worth while to have a good endocrinologist study the case

DR PAUL D FOSTER I think that one should consider some type of trichotillomania The scalp had a mild amount of seborrhea The hair appeared to be entirely normal I believe that it is entirely possible for this girl to cause this condition

DR J WALTER WILSON I did not look on this as a case in which each individual hair grows a certain number of inches and then stops growing I thought that each individual hair had a shorter length of life than normal before falling out

DR SAMUEL AYRES JR Dr Wilson's remarks are correct I approached the case skeptically when the mother said that the hair fell out, but the hairs can be taken in the hand and they come out easily They grow a certain number of inches and fall out, and new ones come in There may be some endocrine factor, but the condition has been present since infancy I should not be at all surprised to see the case become one of alopecia totalis when the youngster gets a few years older I do not know what to do for it

#### Comedonicus Nevus of Extensive Distribution Presented by DR NELSON PAUL ANDERSON

L N a white woman aged 22 years has had an eruption since birth on various areas of the right side of her body These areas had the recurrent formation of "pimples" This complaint was not accompanied with any ill health

The dermatologic examination showed an extensive comedo nevus involving the right side of the neck, upper part of the chest, back of the neck and outer aspect of the upper right arm as well as the right side of the trunk and right leg

An interesting feature of the case is that the nevus seems to be extending. One hundred and fifty thousand units of vitamin A are being given daily in the hope that the follicular keratotic elements of this disease may be favorably modified even as follicular keratotic elements of keratosis pilaris are benefited by that therapy.

## DISCUSSION

DR NELSON PAUL ANDERSON This lady presents an extremely extensive comedo nevus. Eight or ten years ago I went over the literature of the world and wrote a paper on this disease. There are no reported cases of an eruption so widespread as this particular one, which involves practically the entire side of the body. A feature that is interesting is that this nevus was apparent at birth and that it is still extending. This continued progression makes one wonder about the pathogenesis of this type of nevus. The patient is certain that in the past five years there has been a good deal more involvement of the body. There must be some factor in the production of a comedo nevus under nervous control.

**Lupus Vulgaris, Treated with Promizole (4,2'-Diaminophenyl-5-Thiazole-sulfone)** Presented by DR NELSON PAUL ANDERSON

R T is a white woman aged 44. Ten years ago she observed a "pimple" on her right cheek, which has gradually enlarged. At first, a spot appeared on the left cheek. Biopsy in 1937 was followed by treatment with electrodesiccation and solid carbon dioxide. Since then, lesions have recurred. In 1938 lesions were treated for the last time until June 1944. At the onset ten years ago, the patient felt run down. She had afternoon fever. In the past year she has been gaining weight and she feels well. Even now she becomes tired easily.

On the upper central part of each cheek, she has a single, brownish, soft but slightly raised and infiltrated patch. The lesion on the right cheek is larger than that on the left. The borders are white in places from depigmentation. Apple jelly nodules are easily demonstrated under diascopic pressure.

Treatment in the past six months has included nine treatments with water-cooled ultraviolet light under pressure. A salt-free diet was ordered. At present the patient is getting Promizole, 0.5 Gm. At first, 4 tablets a day were given. This dosage was increased at weekly intervals at first to 6 a day, and now she is getting 8 tablets each day.

## DISCUSSION

DR NELSON PAUL ANDERSON Promizole is one of the new sulfonamide drugs. The two earliest drugs of this group are Promin (p,p'-diaminodiphenylsulfon-N,N'-didextrose sulfonate) and Promizole. They belong in the sulfonamide group and apparently have a therapeutic action on acid-fast bacilli.

DR KENDAL FROST I hope that Dr. Anderson will bring the patient before the society again after she has had some treatment. There is little opportunity to see such cases in this locality.

DR SAMUEL AYRES JR I should like to ask whether a tuberculin test was done on this patient.

DR M. E. OBERMAYER While I do not doubt the correctness of Dr. Anderson's diagnosis, I suggest a biopsy to rule out the possibility of sarcoid. In view of the interesting therapeutic experiment with Promizole, histologic confirmation of the diagnosis appears to be especially desirable.

DR NELSON PAUL ANDERSON The reason I have not performed a biopsy is that Dr. Julius Scholtz did so before her treatment with electrodesiccation, which substantiated the diagnosis of lupus vulgaris. I did not feel justified in asking her for another biopsy. I am sure the previous tissue is available for present study.

NOTE—A tuberculin test was done after the patient's presentation, and the reaction was strongly positive.

A Case for Diagnosis (Seborrheic Dermatitis?) Presented by DR ANKER K JENSEN

E B is a young white woman aged 24. She served as a nurse with the armed forces in New Guinea for eight months, from December to July. After three months an infection developed in the right ear. About the same time she had two infections on her right fingers. Soon these infections extended to include the axillary and groin regions. Still later the entire trunk and extremities became covered with an erythematous, weeping, scaling eruption. For a while there was edema of the legs.

She returned five months ago. While returning, aboard ship she had her first attack of malaria. Occasional attacks of diarrhea were experienced while she was in New Guinea. This symptom became severe on her way home.

She weighed 92 pounds (41.7 Kg) when she was received at a hospital in California. Now she weighs 73 pounds (33.1 Kg). Her normal weight before her illness was 104 pounds (47.2 Kg).

Medication at present includes bismuth and opium mixture for control of the diarrhea. Quinacrine hydrochloride (atabrine) is taken for the present control of malaria. A mixture of hydrous wool fat and cold cream is applied locally, and oatmeal baths are taken daily.

DISCUSSION

DR THOMAS NISBET: I saw this girl in New Guinea, just before her return. She had an extensive erythematous, vesicular eruption, which tended to be exfoliative. Her condition should be classified with a new entity seen "out there." It occurs in erythematous form and in an atrophic lichenoid form. This is an eczematoid form of that syndrome. Lichenoid lesions develop at times. It looks like a seborrheic dermatitis at this time. This is true in a good many of these cases. The history of this case is that the eruption began on her hand and ear. The eruption ordinarily does not occur on the ears and about the eyes. She is minus one third of her eyebrows. Loss of weight goes along with it. The prognosis is generally good. The patients get well when they return to a temperate climate. This girl is one of the few who have not responded so favorably to this change of climate.

DR M E OBERMAYER: May I suggest that this eruption conforms with the French concept of seborrheid?

DR THOMAS NISBET: The only thing against the diagnosis of seborrheic dermatitis for persons with seborrheid is that pigmented, lichenoid eruptions develop and sometimes stomatitis as well. Sometimes lesions indistinguishable from lichen planus develop.

DR MILTON GOLDMAN (by invitation): I thought of the possibility of atopic dermatitis which had flared up on account of her illness. She said that her brother had asthma when young.

## Book Reviews

**The Chemistry of Leather Manufacture** By George D. McLaughlin, Edwin R. Theis and collaborators. Third edition. American Chemical Society, Monograph Series 101. Price, \$10. Pp. 789. New York: Reinhold Publishing Corporation, 1945.

Leather chemists have contributed much to the dermatologists' knowledge of the chemistry of the skin. Leather, too, is of interest to the dermatologist because allergic dermatitis from contact with it is no rarity. Both of these facts make this book by McLaughlin and Theis and their collaborators a valuable reference book in the dermatologic field. The book is a third edition on this subject in the American Chemical Society Monograph Series. It brings up to date, it is to be presumed, the subject matter presented in the earlier editions as authorized by John Arthur Wilson.

**Physical Chemistry of Cells and Tissues** By Rudolf Hober and collaborators. Price \$9. Pp. 635. Philadelphia and Toronto: The Blakiston Company, 1945.

This book by Hober and his collaborators is for the advanced student of physical chemistry. For the dermatologist with an adequate background to understand this presentation many of the eight sections of this book should prove helpful. The authors are thoughtful enough to include in the introduction a list of elementary textbooks, a perusal of which would prepare one to understand what this book offers.



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## DERMATITIS OF THE HANDS DUE TO ATOPIC ALLERGY TO POLLEN

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**D**ERMATITIS of the hands (eczema) as the sole or major manifestation of inhalant pollen allergy heretofore has not been reported. Since the causative allergens are borne by the blood it constitutes a localized atopic dermatitis. Sensitization resides primarily in the cells of the capillaries of the skin, in contrast to sensitization in the epidermal cells in contact eczema. This atopic dermatitis of the hands due to pollen allergy occurs, or is exaggerated, during the pollen season, coming, as a patient said, "with the plants." It usually occurs on the dorsal of the hands or on the knuckles and on the dorsal and sides of the fingers and between them, and less often on the palms and around the wrists. Usually it is bilateral and fairly symmetric, varying in degree and extent on each hand. Frequently, especially with its yearly recurrences, other areas of the skin may become affected in varying degrees and in the following approximate order of frequency: the cubital areas, the flexor surfaces of the forearms and lower parts of the arms, the face, especially the eyelids, around the mouth, the chin, sides of the jaws, all surfaces of the neck, the "V" of the chest, the upper part of the back and shoulders, the legs and ankles, the popliteal areas, the inner parts of the thighs, the axillas and, during exaggerated spells, the rest of the skin.<sup>1</sup>

In the last eight years I have studied more than 180 cases of eczema of the hands as a major or sole manifestation of atopic dermatitis. In approximately 16 of these cases eczema has been due to pollen allergy and 6 of these are summarized in this article. In a forthcoming article<sup>2</sup>

1 In 1937 I reported atopic dermatitis due to pollen, food or other inhalant allergies involving the areas mentioned in varying degrees, and I tabulated observations on 30 cases (Rowe, A. H. *Clinical Allergy*, Philadelphia, Lea & Febiger, 1937). I discussed this subject again in 1939 (Rowe, A. H. *Discussion on Atopic Dermatitis, I Allergy*, 11:203, 1939) and since then in other publications. Feinberg also discussed it in 1939 (Feinberg, S. M. *Seasonal Atopic Dermatitis: The Role of Inhalant Atopens*, *Arch. Dermat. & Syph.* 40:200 [Aug.] 1939).

2 Rowe, A. H. *Dermatitis of the Hands (Eczema) Due to Food Allergy*, to be published.

the predominance of food allergy as a cause will be reported. Allergies to animal emanations, dust and miscellaneous inhalant allergens also must be considered as probable though rare causes. One case of symmetric dermatitis of the palms due to inhalant allergy to tobacco has been observed. Though I do not encounter many cases of contact dermatitis of the hands, so frequent in industrial and other occupations, it is my opinion that some so-called industrial causes are secondary activators of atopic dermatitis which is primarily due to food and less often to inhalant allergens. It also appears that such atopic allergy at times is responsible for dermatitis of the hands assumed to be due to infection from or to allergy to fungi.

#### DIAGNOSIS OF POLLEN ALLERGY

As in all clinical allergy, the sole evidence of pollen sensitization may be obtained from a careful examination of the patient's history.<sup>3</sup> The onset or decided exaggeration of dermatitis of the hands during the pollen season is especially suggestive. Pollen as a cause of dermatitis also is possible when a history of present or past hay fever or asthma, probably due to pollen allergy, is revealed in the patient's or even in his familial history. Such a positive history, however, may be absent.

Testing of the skin with all pollens inhaled by the patient is important. With less frequency than in food allergy,<sup>4</sup> negative reactions may occur to pollens responsible for dermatitis. The degree of positive reactions, moreover, does not necessarily indicate the clinical importance of the pollens. Testing should be done first by the scratch method. Since severe exaggeration of the dermatitis, even generalized in type, has occurred after intradermal testing, I usually forego intradermal testing in patients with atopic dermatitis due to probable inhalant allergy. If this testing is performed, weak dilutions are utilized and exaggeration of the dermatitis is always anticipated. Positive reactions of the skin by either test do not necessarily indicate clinical sensitization.

Residence in a room with an efficient pollen filter is valuable not only for diagnosis but also for treatment of atopic dermatitis due to pollen allergy. Relief may not be evident, however, for two to seven days. Probably this is because of the persistent absorption of pollens retained in the depths of the bronchial tract and even in the gastrointestinal tract, but also because of the continued but diminishing allergens in the blood and the body tissues for several days or probably, in some patients, for longer periods, even when the patients remain in an environment relatively free of pollen.

3 Rackemann, F. H. History Taking in Allergic Diseases, *J. A. M. A.* **106** 976 (March 21) 1936.

4 Rowe, A. H. The Evaluation of Skin Reactions in Food Sensitive Patients, *J. Allergy* **5** 135, 1934.

Assurance that pollen allergy is the major or sole cause finally depends on the obtaining of good results from hyposensitization, as is discussed later

#### DIAGNOSIS OF ASSOCIATED ALLERGIES

*A History* Although dermatitis of the hands reported in this article is due to atopic allergy to pollen as the sole or major cause, the possible concomitance of other inhalant, infectant or contact allergies must be remembered. To determine such possible allergies, history again is of paramount value. Thus, nasal or bronchial symptoms, past or present, or exaggeration of the dermatitis from exposure to animals or to the many miscellaneous inhalants, requires their consideration as a contributing cause of the dermatitis. Food allergy should be suspected when any of its possible manifestations are evidenced in the patient's history or when a history is obtained of dislikes for specific foods or of their disagreement with the patient. Moreover, if the dermatitis is exaggerated or if it occurs only during the fall, winter or spring months, food allergy is definitely suggested.<sup>5</sup> Dermatitis due to ingested seasonal foods, especially to fruits and vegetables, also may occur. Possible allergy to oral or injectant drug or medication as a complicating cause also must be remembered. "Id" reactions from bacterial and especially from fungous infections also may cause or complicate dermatitis of the hands.

Contact allergy due to the oils or resins of vegetables, fruits and the leaves and flowers of grasses, weeds, trees, shrubs and plants may be the sole cause of dermatitis, especially of the hands, or it may be an associated cause of dermatitis primarily due to atopic allergy to pollen or food. Detailed questioning and the recording of evidence suggestive of contact allergy of any type are most important.

*B Tests of the Skin* When inhalant allergy other than to pollen is suspected, important information may be obtained by cutaneous testing. The initial use of the scratch test, care with the intradermal test and the fallibility of the results of such tests already discussed in reference to pollen allergy must be remembered. The value of rooms free from dust and inhalants for the study and treatment of all types of inhalant allergy also is evident.

When food allergy is suspected, the evaluation of definite reactions obtained by the scratch method to foods is important. The fallibility of such positive reactions, and especially of negative reactions in patients sensitive to food, and the usual necessity of trial diets, such as my standardized elimination diets,<sup>6</sup> no longer need emphasis. The use of these diets is discussed later in this paper.

<sup>5</sup> Rowe, A. H. Seasonal and Geographic Influences on Food Allergy, *J. Allergy* **13** 55, 1941.

(Footnotes continued on next page)

Possible contact allergy, of course, requires confirmation with patch test, using the substances in question. The proper interpretation of such tests and the occurrence of negative reaction are discussed in current textbooks.

#### TREATMENT OF POLLEN ALLERGY

Control of dermatitis of the hands, as of other areas of the body, when it arises from allergy to inhaled pollens, requires hyposensitization with antigens which contain all the pollens that may be producing the dermatitis. As has been previously stated, the reactions of the skin to all or some of the causative pollens may be negative, therefore I include in the antigen all those pollens steadily encountered by the patient during the months when the dermatitis persists. Thus, dermatitis present during the spring and summer necessitates an antigen containing all the common pollens of trees and grass of early summer, dermatitis in the fall requires all the pollens of late summer and fall and dermatitis continuing from early spring until late fall requires all of the air-borne pollens encountered during those seasons. If allergy to the pollens of cultivated flowers is indicated by history or by testing of the skin, the important ones can be included in the antigen or administered separately. Since I have determined that good results from hyposensitization with pollens usually require very weak dilutions<sup>7</sup> and that concentrated antigens and the stronger dilutions often exaggerate or reestablish the dermatitis, it is unnecessary to limit the number of pollens in the antigen in order to administer eventually large numbers of units of all pollens included in the antigen. Thus, from twenty to fifty pollens usually are combined in one antigen employed in the treatment of my patients afflicted with atopic pollen dermatitis.

Gradually, I have become assured of the usual necessity of minute doses of these "multiple antigens" for the gradual control of dermatitis due to pollen allergy. This especially is necessary for coseasonal treatment which at times must be continued for many months in western states during those periods while pollen remains in the air. The justification of these minute doses resides in the good results obtained in cases of pollen dermatitis treated by me in increasing numbers during the last decade.

Treatment is started with 0.1 cc of a dilution varying from 1:5,000,000 to 1:5,000,000,000, the dilution depending on the severity of the dermatitis, the amount of pollen in the air and the age of the patient. If fewer than twenty pollens are in the antigen, correspondingly weaker dilutions may be required. Injections are given every one

6 Rowe, A. H. *Elimination Diets and the Patient's Allergies*, ed. 2, Philadelphia, Lea & Febiger, 1944.

7 Rowe (footnotes 1 and 6).

to three days and often are administered by the patient. Danger of a general reaction is absent because of the weak dilutions. An increase in the itching and the degree of dermatitis after an injection usually indicates an excessive dose, a decrease in the itching and amelioration of the dermatitis in two or three weeks indicates proper dosage, whereas no change justifies a weaker or a stronger dilution until a beneficial dose is found. When there is decided improvement the dose can be gradually increased, especially after the pollens decrease in the air, but a reduction in dosage becomes necessary should the dermatitis at any time become exaggerated. When pollen leaves the air the successively stronger dilutions of the antigen may be tolerated. On the return of the allergenic pollen to the air, hyposensitization may have been attained, so that the 1/500, and rarely the 1/50, dilution can be continued one or two times a week with no return of the dermatitis. During the pollen season, reduction in dosage to a 1/50,000 or even a 1/50,000,000 or a weaker dilution usually becomes necessary. Indeed, I have obtained excellent results with the perennial injection of dilutions no stronger than 1/5,000,000,000. If the dermatitis is well controlled or absent after one or preferably two years of therapy, injections may be stopped with the understanding that they will be resumed if the dermatitis recurs. As in seasonal hay fever, pollen therapy may be necessary for many years.

#### CONTROL OF ASSOCIATED ALLERGIES

When food allergy is suspected, my elimination diets,<sup>6</sup> modified by a history of definite food dislikes or disagreements and by definite skin reactions to specific foods obtained by the scratch tests, have been utilized for the study and continued control of such allergy. Because of the fallibility of the cutaneous tests,<sup>4</sup> especially for the determination of food allergy, test-negative diets usually fail in the control of such allergy.

For successful treatment by use of elimination diets I have stressed the following recommendations. The prescribed diet may have to be continued for two to three weeks before evidence of improvement is noticed. This is due to the continued presence of the food allergens in the blood and tissues for more than a few days and the persistence and degree of changes in the skin resulting from atopic dermatitis. Moreover, the exclusion of allergenic foods must be 100 per cent, since a maximum degree of allergy must be assumed for all excluded foods until the eczema is satisfactorily relieved. Thus, the patient must be given detailed menus and necessary recipes for bakery products so that accurate use of the elimination diet will be assured and nutrition properly protected.

As previously stated, dermatitis of the hands due to atopic allergy to inhalants other than pollens apparently is rare. It must be considered, however, in resistant cases especially when other manifestations due to

such inhalants are present. Methods of diagnosis already have been discussed. Treatment requires elimination of the specific inhalants from the patients' environments and specific hyposensitization, using very dilute antigens as I now advise for pollen therapy.

Association of an "id" eruption due to allergy to fungi on the feet or other areas of the skin, or a superimposed fungous infection in the area of atopic dermatitis, might occur. This would require proper treatment of the original infection with possible hyposensitization with dilute trichophytin and oidiomycin, or less often with an autogenous fungus antigen.

Contact allergy to various substances which may be associated with atopic dermatitis due to pollen allergy already has been discussed. When it is present, avoidance of the incriminated substances becomes necessary. When allergy to the resins of vegetation is indicated by definite patch reactions, the oral administration of the reacting resins diluted in a vegetable oil may produce hyposensitization, as reported especially by Shelmire.<sup>8</sup> When allergy to the pollens of such vegetation also is indicated by history, with or without positive reactions, I have obtained good or excellent relief from the dermatitis with specific pollen hyposensitization without the oral administration of the reacting resin itself.

#### LOCAL THERAPY

When papulovesicular lesions with oozing, crusting and pruritus are present, continuous compressing or bathing with solution of aluminum acetate diluted 30 to 60 times, often is beneficial. Isotonic solution of sodium chloride, or even tap water, may be used in a similar manner. Between applications of the compresses, or after oozing has ceased, white petrolatum or liquid petrolatum may be applied locally and may relieve the dryness and other discomforts of the skin. Other ointments and lotions, as advised by dermatologists, also may be helpful. Roentgen ray therapy usually will relieve the itching and decrease the dermatitis. Such treatment must be administered only by qualified physicians and with standardized roentgen tubes, however, a total of no more than two units to any one area during a patient's lifetime can be safely administered.

As hyposensitization with proper pollen therapy increases and as other allergenic causes, if present, are controlled, the need for local therapy will decrease and finally disappear.

#### REPORT OF CASES

CASE 1—Mrs W H E, aged 56, first was seen by me in April 1942, at which time she had a recurrent vesicular, oozing, crusting, itching and cracking

8 Rowe.<sup>5</sup> Shelmire, B. Contact Dermatitis from Weeds. Patch Testing with Their Oleoresins, J A M A **113** 1085 (Sept 16) 1939

eruption of seventeen years' duration on the dorsa of both hands and between all the fingers. The onset was in February or early March of 1925, in Santa Barbara, where she had lived for three years. She took up residence in Bakersfield in 1938, and the eruption recurred early each March, reaching a maximum during the period from April to October, decreasing in November and December and being absent from late December until early March.

Four physicians were consulted, from 1926 to 1935, who tested her by the scratch and contact methods. No positive reactions, except to Crisco, occurred. In 1941, skin testing with 180 inhalant and 160 food allergens produced negative results. All types of treatment, including much roentgen ray therapy, had failed. No history of hay fever, asthma, bronchitis, sick headaches, indigestion, previous dermatoses or any other possible manifestation of allergy was obtained. In 1940, for the first time, the dermatitis involved the forearms, neck, face, groin, legs and ankles. These areas also were involved in 1941 to a moderate degree, but the major manifestation had continued on the backs of the hands and around the fingers. The palms were never involved.

Her dietary history revealed no dislikes or idiosyncrasies for any food. Itching and burning of the hands, however, had occurred when in contact with fresh fruit and vegetables, especially with tomatoes.

There was no history of an allergy to any drug or chemical.

Her sister and brother suffered with bronchial asthma and her son had mild bronchial allergy. Her menstrual periods had been absent for six years. No tobacco or alcohol was used.

Her physical examination revealed no abnormalities except for the dermatoses previously mentioned.

Cutaneous testing with all important food and inhalant allergens gave no reactions by the scratch method. Intradermal testing with inhalants was negative. Patch tests with thirty-six oils and resins gave reactions of 3 plus to mugwort and *Franseria acanthicarpa* and a reaction of 1 plus to poverty weed and camomile.

*Treatment and Progress*—Hyposensitization with an antigen containing forty-two important pollens from the Bakersfield area was initiated with hypodermic injections of 0.1 cc of a 1:5,000,000 dilution given every two days. In two weeks there was definite improvement. The dose then was increased by 0.1 cc at each injection with a resulting increase in the dermatoses when 0.5 cc was administered. The dose then was reduced to 0.05 cc of the 1:5,000,000 dilution and repeated every two days. The patient returned from Oakland to Bakersfield on May 27. There was complete relief from the dermatitis of the hands. An increase to 0.1 cc had produced an increase in the eruption on two occasions in the previous month. In mid-October, however, 0.1 cc was tolerated with complete control of her eczema. In late October and through the winter months, injections were continued every two to three days with a gradual increase up to 0.6 cc of the 1:50,000 dilution. In April 0.1 cc of the 1:5,000 dilution caused itching of the hands and a slight eruption. In the summer and fall of 1943 injections were continued with 0.4 cc of the 1:50,000 dilution with no recurrence of the eruption. Intolerance of a larger dose was indicated by slight itching. During the winter of 1943 and the entire year of 1944 treatment was continued with the 1:5,000 dilution up to 0.2 cc every five to seven days, with complete control of the patient's dermatitis on all areas of the body.

Because of the positive patch test reactions to the resins of the various vegetations recorded earlier, a 1:100,000 dilution of a mixture of these resins in sesame oil was given by mouth, beginning with one drop and increasing gradually to eight drops daily. This treatment was continued for a period of three months.

and has not been resumed in the last two years. Moreover, in March 1944 slight eruption occurred on the fingers, palms, backs of the hands and around the wrists on two occasions immediately after lettuce had been handled.

CASE 2—Mrs L. G., aged 32, was first seen in April 1937. She had had a dermatitis in the palms of the hands for eighteen years. It appeared in early February and continued until May or June. During the other months the palms were either smooth or slightly scaling and rough. The dermatitis always started with vesicular papules and pruritus with consequent excoriations, oozing and crusting. Thickening, cracking and scaling in varying degrees were constant. The recurrence of the dermatitis in the spring months always had been associated with multiple papulovesicular lesions. In no other area did the skin become involved until the last two months, when the forearms and neck became covered with an erythematous crusting and thickened dermatitis. There was also an erythematous scaling dermatitis on the ears and a moderate eruption on the arms and forearms.

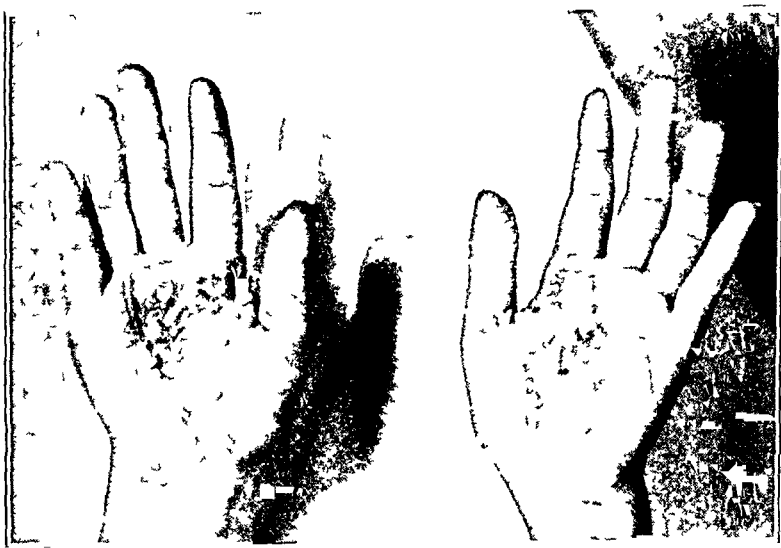


Fig 1—Atopic dermatitis of palms recurring from early February to mid-summer for eighteen years.

There was no history of hay fever or asthma except sneezing and nasal congestion during two winters. Recurrent sick headaches, chronic indigestion and other symptoms suggestive of an allergic cause were absent.

Physical examination indicated nothing abnormal. No dermatophytosis was present. The blood count, complement fixation and urinalyses showed that in these respects the patient was normal.

Cutaneous testing by the scratch method revealed no reactions to any food allergens or to any pollens of trees or of grasses or weeds or of cultivated flowers or to any animal emanation, house dust or miscellaneous allergens with which tests were made. Reactions to patch tests with the resins of the leaves of acacia, elm, *ny*, oak, magnolia, brome, ray and bermuda grass, coastal sage, mugwort, Western ragweed, cocklebur and helenium were negative.

Because of the occurrence of the dermatitis in the spring months it was assumed, in spite of the negative skin reactions, that blood-borne allergens from inhaled seasonal pollens were responsible for this cutaneous allergy. Therefore an antigen which contained all of the common pollens of trees, grass and early summer weeds



native to her community was prepared. Treatment was started with a 1:5,000,000 dilution. Subcutaneous injections were given two or three times a week and increased in the usual manner. The itching, extent and degree of the dermatitis decreased during the next two months. By fall, 0.6 cc of the 1:50 dilution was being given every five to seven days, and this dose was continued. There was no return of the dermatitis after 1937, although during the springs of 1940 and 1941 a slight roughness and a few occasional papulovesicular lesions in the palms occurred. Because of the absence of all dermatitis in the spring of 1942, hyposensitization was stopped in June.

There was no recurrence of the dermatitis, except slight roughness and scaling in the palms, from the spring of 1942 until late February 1944, when the usual lesions rather rapidly reappeared. Pollen therapy was reinstituted with a 1:50,000,000 dilution of the antigen, as administered in 1937. Gradually the doses were increased during the summer and fall months. By November, when her hands were entirely clear, 0.1 cc of the 1:5,000 dilution was being given every seven days. This dose will be increased gradually up to the 1:50 dilution if tolerated and perennial therapy every seven to fourteen days will be advised possibly for two or more years. To conserve time and expense, self administration of the antigen under my supervision will be justifiable.

When the patient was first seen in April 1937, because of the possibility of food allergy as an associated cause of the dermatitis, my cereal-free elimination diet was prescribed. With improvement, important foods gradually were added, and by August a general diet was ordered. This general diet with a moderate reduction in milk, eggs and wheat was continued until April 1944, one and one half months after the resumption of pollen therapy. Then, because of delay in the disappearance of the dermatitis and because of the initial use of the cereal-free diet in 1937, this diet again was prescribed with evidence of benefit in the ensuing two months. Since then, food allergy, in a secondary role to pollen allergy, has been demonstrated on several occasions by an obvious increase in the dermatitis with the addition of milk or eggs to the diet. As in 1937, this food allergy may become gradually suppressed by the continued pollen therapy, so that moderate amounts of milk and eggs can be eaten again without resultant dermatitis.

CASE 3—Mrs. C. C., aged 32, was seen first in July 1943. In July 1940 she had had an itching, vesicular, oozing, and later a crusting eruption on the palm of each hand, on the sides of most of the fingers and, to a moderate degree, on the dorsum of the right hand and the dorsa of the fingers. Soon the same areas of the left hand were affected. The dermatitis disappeared in mid-September. It reappeared in March and lasted until late October, being exaggerated from late June until September. The dermatitis reappeared in late February of 1942, continuing until early November with an occasional eruption on the right hand during the winter months, especially after the washing of dishes or clothes. In 1943 the same dermatitis on the hands and fingers and especially on the palms reappeared in early March and persisted with increasing severity until I saw her in July. For the first time, during the three weeks preceding this first visit, she had had a scaling, erythematous eruption around the mouth, on the sides of the nose and on the jaw.

She gave no history of seasonal or perennial nasal allergy, bronchial allergy, gastrointestinal symptoms or any other indications of possible clinical allergy. Her dietary, drug and environmental histories were negative from the allergic viewpoint. One sister had had eczema of the hands, arms and forearms for about twelve years. One child had popliteal eczema in infancy.

She had lived in Sacramento until November 1942 and for the last eight months in Oakland

Her physical examination revealed nothing abnormal except the dermatitis of the hands, especially of the palms, and the lesser dermatitis of the face as noted in the history. Her blood pressure was 100 systolic and 70 diastolic

Analyses of blood and urine gave normal results

Testing of the skin with all important animal emanations, miscellaneous inhalants, stock house dust allergens and all important pollens of trees, grasses, weeds and cultivated flowers by the scratch method elicited negative reactions. Patch tests with the resins of the leaves of mugwort, coastal sage, Western ragweed, cocklebur, helenium, marigold and camomile elicited negative reactions after forty-eight hours

*Treatment and Progress*—Because of the occurrence of this dermatitis during the spring, summer and fall months, atopic allergy arising from blood-borne allergens from inhaled pollens was assumed in spite of the negative skin reactions. Therefore, an antigen which contained thirty-eight of the important pollens of trees, grasses, weeds and cultivated flowers present in the air of the community in which she resided was prepared. An initial dose of 0.1 cc of a 1:5,000,000 dilution was administered three times a week during the first three months. For the first week compresses were applied to the hands for an hour, three or four times a day, with a 1:40 dilution of solution of aluminum acetate. Since then compresses have not been necessary. The dermatitis disappeared from the face in two weeks, and the eruption was practically absent from the hands in one month. In September a moderate eruption reappeared on the dorsa and palms of the hands. In October an occasional small vesicle with slight scaling occurred on the palms and the sides of the fingers. During November the eruption was practically absent except for a moderate amount on the sides of the fingers and on the palms. This slight eruption was due to the discontinuance of the antigen for about ten days, or possibly to the handling of a Christmas tree. In February 1944 no dermatitis was present except a moderate cracking and scaling eruption 1 by 2 inches (2.5 cm by 5 cm) on the right palm and 1 by 1 inch (2.5 cm by 2.5 cm) on the left palm.

Gradually, during the winter months, the dose of the antigen had been increased to 0.1 cc of the 1:500 dilution. Because of the slight persisting dermatitis on the palms in early March, a decided reduction, to 0.1 cc of the 1:5,000,000 dilution every two or three days, was ordered, and one month later the dose was reduced to 0.1 cc of the 1:50,000,000 dilution. Thereafter the degree and area of palmar involvement decreased, so that in August the patient stated that there was "easily 90 per cent less dermatitis than one year previously." In that month she worked for two weeks in the garden, her hands being covered with gloves, without any increase in the eruption in her palms. During the next six months the dermatitis practically disappeared, though a slight increase occurred when the dose was increased to 0.5 cc of the 1:50,000,000 dilution. It again decreased to an absolute minimum with the continued administration of 0.3 cc.

The patient has discovered that a moderate eruption occurs on the palms when she handles squash recently picked from the vine, though she can handle squash without any eruption twenty-four hours after it has been picked. Moderate exaggeration of the dermatitis, moreover, occurred when, after painting furniture, she removed paint from the skin of her hands with turpentine.

CASE 4—Mr. F. O., 25 years of age, first seen in March 1941, had experienced, in September three years previously, an itching, papulovesicular eruption with

later oozing and crusting on the dorsum of the right index finger. This eruption decreased through the winter and disappeared in March. The eczema reappeared in the following September on the dorsum of the right hand, on the sides of three of its fingers and on the ventral surface of the right wrist. It again disappeared one month later, soon after the patient left the Sacramento Valley for New York. Again it was absent until July or August of 1940. Then the eruption reappeared on the dorsum of the right hand, steadily increasing to a maximum in December and January when the dorsa of both hands and the dorsa and sides of all fingers became involved, with pitting of all the finger nails.

The patient gave no history of any previous eruption except for slight attacks of poison oak up to ten years ago. He also had suffered from moderate hay fever in the spring months.

His dietary history indicated no food dislikes or disagreements.

He had always lived in Sutter County in the Sacramento River Valley of California and had observed a rapid improvement in his dermatitis on visiting near the ocean. The eruption first developed three years ago when he moved from town to his prune and peach ranch. He gave no familial history of allergy.

His physical examination indicated nothing abnormal except for a rough cracking, scaling type of eruption on the dorsa of both hands and of all fingers, on all surfaces of both wrists with scattered patches on the forearms and a few on the arms. The nail of the right index finger was thickened, and pitting was present in the periphery of the other nails. The rest of the skin was free of eruption except for maceration between the third and fourth right toes. Analyses of his urine and blood gave normal results, with 3 per cent of eosinophils.

Cutaneous tests by the scratch method with all important food allergens elicited negative reactions. Reactions of 2 to 4 plus were obtained to many grass pollens, to amaranthus, atriplex, white goose foot, pickleweed, sugar beet, Russian thistle, Western ragweed, oak, eucalyptus, chrysanthemum, coreopsis, cosmos, alfalfa and especially to olive pollens. Reactions of 1 or 2 plus occurred to goose and duck feathers, dog hair, orris root, cottonseed and glue. Intradermal testing with 1:1,000 dilutions gave reactions of 1 and 2 plus to many other pollens, animal emanations, miscellaneous inhalants and house dust allergens. Skin tests with twelve feed and grain allergens were negative. Patch tests with the resins of twenty grasses, weeds and shrubs were negative except for a 2 plus reaction to camomile.

Atopic pollen allergy was indicated by the onset of the dermatitis in the summer and fall months for three years, by the improvement on coming to the ocean area, and by the many skin reactions to pollens of all types. Therefore an antigen containing all the important pollens of trees, grass, weeds and flowers was prepared. Treatment was started with 0.1 cc of the 1:5,000,000 dilution. Injections were given every two days, repeating and gradually increasing subsequent doses. Compresses of a 1:40 dilution of solution of aluminum acetate were applied. There was gradual improvement in the first three weeks. Then a decided exacerbation occurred, apparently after the injection of 0.3 cc of the 1:500,000 dilution of the antigen. The patient was hospitalized for five days in an air-conditioned pollen-free room, compresses were applied and injections stopped. Thereafter injections were continued with 0.1 cc of the 1:5,000,000 dilution, with a subsequent increase to 0.3 cc, two times a week until September. Thereafter until December injections were given every five to seven days, after which pollen therapy was discontinued. No eruption has occurred since then except for a slight amount in the fall of the next year, when pollen injections were resumed for one month, and for a moderate

eruption one and a half years later in March and April, because of the latter eruption pollen treatment again was given, with complete control in a few weeks.

Since eczema due to food allergy may occur or may be exaggerated only from September to May,<sup>5</sup> and especially in the winter months, it was necessary to consider food allergy as a major or complicating cause of the persistent hand eczema which occurred in the winter months of 1940-1941 in this patient. My cereal-free elimination diet therefore was prescribed. Because of rapid improvement, the patient was given a general diet at the end of six weeks. During the last four years the dermatitis has been controlled with pollen therapy without the elimination of any food.

**CASE 5**—Mr L. S., aged 55, had had a scaling, cracking, itching nonoozing dermatitis with intermittent vesiculation and crusting on the ends and palmar surfaces of the fingers of the right hand, and moderately of the left hand, and on the fifth right knuckle and the right lateral thenar area for the last five years, starting during early August and lasting until December, being definitely exaggerated in September. In addition, patches of similar dermatitis had occurred on the anterior portion of the legs, the popliteal areas and the outside of the ankles. Pruritus ani and itching and oozing in the auditory canals had developed for the first time that fall.

Hay fever had occurred during the first thirty-five years of the patient's life in the San Joaquin Valley from early May until mid-July and to a lesser degree in the San Francisco Bay area since then. There was slight asthma also with the hay fever at the age of 30.

His dietary, drug and environmental histories were negative from the allergic viewpoint. His father suffered with seasonal hay fever.

Physical examination revealed no abnormalities except for the dermatitis mentioned before and a reddened edematous nasal mucosa. Blood, urine and complement fixation blood tests indicated no abnormalities.

Testing of the skin revealed positive reactions to all the grass pollens, to most of the tree pollens and to pollens of several of the summer and fall weeds and cultivated flowers with which tests were done.

*Treatment and Progress*—Treatment was started on Aug. 20, 1943, with 0.1 cc. of a 1:50,000,000 dilution of a multiple pollen antigen containing forty of the pollens of spring, summer and fall in his community. The doses were gradually increased, and each dose was repeated two or three times. On November 12 the 1:5,000,000 dilution was started. Dermatitis of the hands had cleared in late December. By Feb. 1, 1944, the 1:500 dilution was administered, and by March 1 the 1:50 dilution was started. During May and July the dose was increased to 0.6 cc. of the 1:50 dilution every five days. Through the rest of 1944, 0.2 cc. of the 1:50 dilution was administered every five days by the patient. With this treatment there has been no return of the dermatitis on the hands or on the legs, or of the pruritus ani.

**CASE 6**—Mrs E. T., aged 37, was first seen in November 1943, when she had an oozing, vesicular dermatitis on the backs of the hands and fingers, and especially on the sides of the fingers, and moderately on the backs of the wrists. There was a moderate-sized area of dermatitis on the inside of the right ankle. For the last ten years this dermatitis had returned each April or May "like the plants," being especially severe from July until late October, then reducing to a minimum in the winter months. The eruption was always moderately exaggerated for several days before each period.

There was no history of previous dermatoses, hay fever or bronchial allergy. Sick headaches had recurred every month for about ten years, but there had been practically none during the last two years.

Her dietary, drug and environmental histories gave no information of help with respect to allergy. Her familial history was negative for allergy.

Analyses of the blood and urine revealed no abnormality. Cutaneous reactions to all important animal emanations, miscellaneous allergens, dust and pollens were negative.

*Treatment and Progress*—Hyposensitization was started with a multiple antigen which contained all the important pollens of spring, summer and fall from the community in which the patient resided. The initial dose was 0.1 cc of the 1:50,000,000 dilution. With self administration of the antigen, the dose was gradually increased to 0.7 cc by March 1, the injections being given every two days. Decided decrease in the dermatitis occurred during the winter months. With the continued administration of the pollen antigen there was no exaggeration of the dermatitis during the late spring or the summer and fall months, though a slight dryness and thickness of the skin of the right hand and a slight dermatitis on the inner side of the right ankle persisted. In September the patient went to Albuquerque, N. Mex., by automobile. On her return to the San Francisco Bay area a decided increase in the dermatitis of the right ankle and dermatitis of the left leg developed. This gradually subsided in the month after her return with local application of solution of aluminum acetate diluted 1:50, and with continued pollen therapy. During the last five months 0.3 cc of the 1:50,000,000 solution of her pollen antigen has been self administered every three days. Dermatitis of the hand has been practically absent.

#### COMMENTS

Though this report is devoted to dermatitis of the hands as the sole or major manifestation of atopic pollen dermatitis, it must be remembered that this type of dermatitis usually involves other areas of the skin, especially the face, neck, shoulders and the upper and lower extremities, as well as the hands. This was illustrated in the tabulation of areas involved in 30 cases in which pollen allergy, along with other inhalant and food allergies, was a major cause, as published by me in 1937.<sup>1</sup> In the last eight years many additional cases of atopic dermatitis affecting multiple areas and due to pollen, and less often to other inhalant allergies, have been studied. As reported in 1937, hyposensitization with pollen antigens, as recommended in this article, and when indicated with hyposensitization to other inhalants and elimination of allergenic foods, usually has produced excellent or good results.<sup>9</sup>

Thus, atopic dermatitis of the hands as a sole or major manifestation of pollen allergy is rare compared with dermatitis affecting the other

<sup>9</sup> As reported in 1937,<sup>1</sup> food allergy alone or complicated in some cases with inhalant, or rarely with infectant, allergies is a common cause of atopic dermatitis, not only in infancy but also throughout life, even in old age. The face and neck and flexures and other surfaces of the extremities especially are involved by such food allergy—the hands often being the site of its major or sole activity, as pointed out previously in this paper.

areas noted and much less common than atopic dermatitis of the hands due to food allergy.<sup>2</sup> This accounts for the comparatively few cases of eczema of the hands due to pollen allergy encountered by me.

Following is an analysis, with comment, of the histories, testing and treatment in 6 cases of atopic pollen dermatitis of the hands summarized in the foregoing pages.

The seasonally recurring or exaggerated dermatitis had been confined to the dorsa of the hands and the dorsa and sides of the fingers for fifteen years, with additional involvement of the face, neck, forearms, groins, legs and ankles for the past two years in case 1, to the palms alone for eighteen years with involvement on the neck, forearms and arms for the last two months in case 2, to the palms, mainly, and to the sides and dorsa of the fingers and, moderately, to the dorsa of the hands for three years, with facial involvement for the last three weeks, in case 3, to the dorsum of the right hand and several of its fingers for three years and to the dorsum of the left hand for several months, with no other skin involvement, in case 4, to the ends and palmar surfaces of all the finger tips with a few patches on the dorsum of the right hand associated with moderate dermatitis on the popliteal areas, shins and outer side of the ankles—all for five years in the fall months—in case 5, finally, to the dorsa of the hands and wrists with a moderate eruption on the inner side of the right ankle for ten years in case 6.

Thus, the dermatitis of the hands in these 6 cases had existed for from three to eighteen years with an average duration of 9.3 years. The dorsa of the hands and the dorsa and sides of the fingers were more often involved than were the palms. The dermatitis was entirely confined to the hands, especially the right one, in case 4, and to the hands alone for fifteen, eighteen and three years before other areas were involved in cases 1, 2 and 3 respectively. Moderate dermatitis on the legs in case 4, and on the ankles in case 6, was continually associated with the major dermatitis of the hands.

Hay fever in the spring or summer months had occurred in cases 4 and 5. Possible nasal allergy during two winters had been present in case 2, and recurrent sick headaches had occurred for ten years in case 6. No history of possible allergy other than dermatitis was present in cases 1 and 3. Thus, the dermatitis discussed in this article may be the only evidence of pollen allergy, and manifestations of other allergies may or may not be present.

The familial history revealed bronchial allergy in the sister, brother and son in case 1, eczema in the sister and 1 child in case 3, and nasal allergy in the father in case 4. The familial histories were negative for allergy in the other 3 cases.

There was concomitant contact allergy in 2 of the 6 cases. Itching from contact with certain fresh fruits and vegetables, especially tomato,

occurred in case 1. Also, in case 1, the patch test elicited reactions of 3 plus to resins of mugwort, franseria, povertyweed and camomile. The significance of these reactions to the patch test is discussed later. A rash also occurred on the palms from freshly picked squash in case 3. The irritation of the palms from turpentine used to remove paint from the hands was due to irritant action rather than to allergy, in my opinion. Patch tests with resins of weeds in cases 2, 3 and 4 elicited negative reactions, except to camomile in case 4, which received no consideration in therapy.

Food allergy was an associated secondary factor only in case 2. During the first few months of pollen therapy, my cereal-free elimination diet was prescribed with apparent help, and this diet again became necessary during the fall and winter of 1944 because of the continued moderate dermatitis during those seasons. In case 4 the elimination diet was used for a brief time, but it soon was discontinued. The existence of recurrent sick headaches in case 6 suggested food allergy as a cause, but it was unnecessary to use trial diet in addition to pollen therapy for the control of the dermatitis of the hands. Negative dietary histories and skin reactions to foods were present in all 6 cases. Both, but especially the negative reactions, often occur in chronic food allergy and emphasize the necessity of trial diet for its study.

Cutaneous tests by the scratch method with all important pollens of trees, grasses, weeds and cultivated flowers elicited negative reactions in cases 1, 2, 3 and 6. Negative reactions to allergenic pollens are commonly reported, even in hay fever and asthma due to pollen allergy, because of which the ocular test has been devised. Positive reactions were obtained to most of these pollens and to several animal emanations and miscellaneous inhalants in case 4, and in case 5 to most of the pollens mentioned earlier. Since all 6 cases were primarily or entirely due to allergy to inhaled pollens, the value of the history of seasonal exaggeration or occurrence of the dermatitis as an indication of pollen allergy in the absence of positive skin reactions is obvious. Scratch tests also have elicited negative reactions to pollens in many patients with atopic pollen dermatitis involving additional skin areas. As already discussed, intradermal tests with pollen allergens are not routine when reactions to scratch tests are negative in these patients, this is because of the possible severe exaggeration of the eruption by the injection of the pollen allergens.

Hyposensitization, as previously discussed, has been accomplished in all 6 cases with multiple antigens containing all the important pollens which were present in the patient's environmental air during those months when the dermatitis was present. All such pollens were included in the antigens, even though skin reactions to them were negative. In

each case a 1 50,000,000 or a 1 5,000,000 dilution was first given. Had infants or young children been treated, weaker dilutions would have been used. In case 1, the doses were gradually increased during the winter months to 0.6 cc of the 1 50,000 dilution. In the spring, summer and fall months 0.4 cc was tolerated, and, since then, 0.1 cc of the 1 5,000 dilution given every five to seven days for one year has prevented a recurrence of the dermatitis. In case 2 a dose of 0.6 cc of a 1 50 dilution finally was reached in the late fall months. This dose was repeated every one to two weeks for five years with excellent results except for moderate dermatitis on the palms in March or April three or four years ago. Treatment was discontinued for two years with no return of the dermatitis. However, palmar dermatitis returned in February 1944, requiring a resumption of pollen therapy, with the gradual production of satisfactory results. In case 3 the dose was gradually increased to the 1 500 dilution in the late winter. Then a moderate return of the dermatitis occurred in the early spring, because of which the 1 50,000,000 dilution again was given. It was then determined that 0.3 cc of this dilution given every three to five days controlled the dermatitis, whereas 0.5 cc caused a moderate exacerbation. In case 4, the 1 500,000 dilution caused a return of the dermatitis, which was well controlled by 0.3 cc of the 1 5,000,000 dilution given every five to seven days. In case 5 the dermatitis gradually came under control with increasing doses of the antigen and with a final dose of 0.6 cc of the 1 50 dilution administered every five days until August. Then, during the fall season, 0.2 cc was given with complete control of the dermatitis. In case 6 good results were obtained and maintained with 0.3 cc of the 1 50,000,000 dilution. Thus the use of the initial weak dilutions of multiple pollen antigens and the eventual control and maintenance of hyposensitization with dilutions varying from 1 50,000,000 to 1 50, according to the patient's tolerance, are illustrated by the results of the pollen therapy in these 6 cases.

Perennial hyposensitization has been given in cases 1, 3, 5 and 6 for one to two and a half years. After continued control for two to four years treatment will be stopped to determine whether lasting protection has been established. The absence of dermatitis for two years after perennial treatment for five years in case 2 illustrates established hyposensitization, but of limited duration. In contrast, comparatively little therapy has been necessary to produce the excellent results in case 4. Thus, the duration of treatment must vary with the individual response in each case to the pollen therapy. As in nasal and bronchial allergy due to pollen, some patients may require therapy more or less constantly for many years. The administration of pollen by the patient facilitates such continued therapy and is justified, especially when repeated doses of weak dilutions are used.



Because of the positive patch reactions to the resins of vegetations in the residence area in case 1, a dilute preparation of these resins was given by mouth during the first few months of hyposensitization with a multiple pollen antigen according to Shelmire's advice. In the last two years, however, pollen therapy alone has maintained excellent control. Similar results with pollen therapy were reported by me in 1937.<sup>1</sup>

#### SUMMARY

1 Dermatitis of the hands as a major or sole manifestation of inhalant pollen allergy is reported for the first time. Twenty-two cases have been encountered. Six case records are summarized.

2 Dermatitis on the face, neck and extremities and less often on the torso also may develop, usually after the major dermatitis of the hands has recurred for several years.

3 Dermatitis of the hands, secondary in importance to the dermatitis of any or all of the aforementioned areas, due to atopic pollen allergy, is more common than is its major localization on the hands as reported in this article.

4 Recognition of food and of other inhalant and infectant allergy, at times secondary to the major pollen allergy, is necessary.

5 The importance of a history of recurrence or exaggeration of dermatitis of the hands during the pollen season and the frequency of negative cutaneous reactions, especially by the scratch tests to the causative pollens, are necessary to remember in diagnosing these cases.

6 There may or may not be a personal history of other allergic manifestations, or a positive familial history.

7 Hyposensitization with multiple antigens containing all important pollens in the air in the patient's environment during the months that the dermatitis exists is advised.

8 The initial injection of weak dilutions of these multiple pollen antigens and the varying maximum doses necessary for the establishment and maintenance of hyposensitization are discussed. Frequently repeated small doses of weak dilutions varying from 1:5,000,000,000 to 1:50,000 are required for good results.

# TREATMENT OF TINEA CAPITIS WITH SPECIAL IODINE AND DILUTE ACETIC ACID

## Preliminary Report of Results

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THE object of this paper is to lay before the members of the medical profession a new form of iodine medication for topical application which it is hoped will prove effective in the treatment of tinea capitis

Numerous topical applications have from time to time been proposed for the treatment of tinea capitis, but all have fallen short of expectations. A treatment which for a while seemed to show promise was that proposed by Kingery,<sup>1</sup> who recommended applications three times daily of a solution of gutta percha in chloroform, containing 0.5 per cent thymol and 1 per cent oil of cinnamon. The hair was to be clipped prior to the treatment, and the application was to be discontinued on appearance of reaction. In the past as well as at present many topical combinations have utilized iodine in some form in the treatment of ringworm, as this remedial agent has been shown to be definitely fungistatic and to a degree fungicidal for the ringworm fungus. Schamberg, Brown and Harkins<sup>2</sup> have demonstrated that iodine in a 1:85 dilution killed *Epidermophyton inguinale* after exposure for only fifteen minutes. Emmons,<sup>3</sup> in a comparison of various fungicidal agents with phenol, found iodine highly effective and assigned to iodine a phenol coefficient of 3,000 against *Trichophyton gypsum* and *Monilia albicans*.

## PRINCIPLE OF THE METHOD

The presence of numerous cases of tinea capitis has prompted the reconsideration of the topical treatment of this disease. Because of

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1 Kingery, L. B. Thymol and Cinnamon Oil in the Treatment of Ringworm of the Scalp, *Arch Dermat & Syph* **20** 797 (Dec) 1929. Loomis, E. C. Ringworm of the Scalp. Treatment with Thymol and Oil of Cinnamon, *ibid* **26** 495 (Sept) 1932.

2 Schamberg, J. F., Brown, H., and Harkins, M. J. Chemotherapy of Ringworm Infection. Preliminary Report, *Arch Dermat & Syph* **24** 1033 (Dec) 1931.

3 Emmons, C. W. Fungicidal Action of Some Common Disinfectants on Two Dermatophytes, *Arch Dermat & Syph* **28** 15 (July) 1933.

the recognition of iodine as a most efficient fungistatic agent, an effort was made to intensify activity through photosynthesis, whereby, it was believed, the iodine molecule could be made a more active molecule (an activated molecule) At the onset of this discussion it is important to bear in mind that the fundamental reaction in photosynthesis is a photochemical one and that for its consummation a number of factors are required

*Source of Energy* The quartz mercury vapor arc lamp was used, with most of its energy in the 2,600 to 2,900 angstrom unit level

*Oxygen and Iron* One of the outstanding characteristics of photodynamic processes is that they occur only in the presence of oxygen Iron must also be present To meet these requirements red blood cells were used, for the function of the red blood cells involves their physiologic oxygen-carrying capacity, and the hemoglobin of the red blood cells, made up of the protein, globin and an iron-containing compound known as heme, supplied the needed iron<sup>4</sup> It has been shown that approximately 1 Gm of hemoglobin will combine with 1.36 cc of oxygen<sup>5</sup> Furthermore, it has been proved that the oxygen uptake during photodynamic action is the same for both intact and hemolyzed red blood cells The supply of oxygen was further enhanced through the use of magnesium dioxide, while sight was not lost of the fact that ultraviolet radiation produces a certain amount of ozone, a form of oxygen

*Catalyst and Photosensitizer* Chlorophyll was used both for its property as an organic catalyst<sup>6</sup> and for its photosensitizing power Chlorophyll through its function as a catalyst can and does accelerate chemical reaction The catalyst in this role remains unaltered, and it does not per se influence the composition of the substance or combination formed Chlorophyll in its role as a photosensitizer promotes oxidation by oxygen

Certain molecules widely different in chemical composition possess the nonspecific ability to photosensitize chemical reaction This consists principally in the ability of the molecule to hold its quantum of absorbed energy of activation more or less intact, thus becoming an activated molecule The molecule to which the energy of activation is transferred may participate in chemical reactions the nature of which is determined by the chemical property of the molecule At certain times the sensitizer molecule may enter into collision with an appropriate molecule of another kind and the energy of activation transferred to the other

4 Harrow, B Textbook of Biochemistry, ed 2, Philadelphia, W B Saunders Company, 1940

5 Blum, H F Photodynamic Action and Diseases Caused by Light, New York, Reinhold Publishing Corporation, 1941

6 Arnow, L E, and Reitz, H C Introduction to Organic and Biological Chemistry, St Louis, C V Mosby Company, 1943

molecule and this becomes disclosed in the photosensitizer molecule through its ability to fluoresce. It is my belief that the iodine molecule photosensitized can become an activated molecule and probably capable of more intensive action and effect.

#### THE MEDICAMENT

The medicament employed in this study is a mixture consisting of iodine crystals, red blood cells, chlorophyll and magnesium dioxide. The final product is reddish black and contains 15 per cent iodine and 0.8 per cent inorganic material. It is used in the proportion of 2 Gm of the iodine to 32 Gm of benzoinated lard. At present, trial is being made of the iodine mixture of the same strength incorporated in an oil. It is believed that such would prove more efficient because of the fact that the iodine to a degree dissolves in the oil and the rest of that iodine, although remaining as a suspension, insures a more even distribution of the medicinal substance. It would also appear that the longer the iodine remained in the oil the greater would be the amount that would go into solution.

#### METHOD OF TREATMENT

The treatment followed in this study consisted in clipping the hair of the scalp and keeping it short. The topical applications consisted in the use of acetic acid and the iodine combination. First, the acetic acid was rubbed into the scalp with a toothbrush for two minutes, special attention being paid to the infected areas. This was followed by keeping an electric bulb of 150 to 200 watt strength sufficiently close to the scalp to impart a distinct sensation of heat. Then the iodine ointment or oil was rubbed into the scalp with a toothbrush or hand for two minutes, and the electric bulb was used again for six minutes.

The acetic acid was used for the purpose of reducing the activity of the ringworm fungus, for it has been shown that this fungus will not thrive in an acid medium. Three per cent acetic acid was chosen, since this strength of the acid was believed to be efficient and proved to be nonirritating. The use of the electric bulb following application of the iodine was for the purpose of possibly inducing some vaporization of the iodine, for substances in a vapor form are rather readily absorbed.

The criteria used for the determination of a cure consisted of direct examinations of the suspected hair and observation of the scalp hair with filtered ultraviolet rays. Both of these methods were used in this series, however, in the first 7 cases only the direct examinations were made. Three consecutive negative observations by both methods

were considered to indicate a cure, and the observations were made at four to five day intervals. It was found that there was a close agreement in the results by the two methods, however, it was observed that at times scales lying rather loose and close to the hair could not always be detected by the filtered ultraviolet rays, and direct examination at times showed such scales to contain the fungus and cultivation of such scales on Sabouraud's medium showed a growth in some instances. It is my opinion that both methods of examination should be used whenever possible, to determine the cure of tinea capitis.

The subjects consisted of 60 children with ringworm of the scalp. In each case the infected hairs were subjected to direct examination and were also cultured on Sabouraud's medium. Of the 27 patients cured, 26 had infections with *Microsporon audouinii* and 1 with *T. gypseum*. The patients were mainly boys and varied in age from 4 to 11 years. The average time required for a cure was four months. Some of the patients of this series are still under treatment.

#### COMMENT

A new combination of iodine is here proposed as a topical application for tinea capitis. This application is used with acetic acid. The latter is for the purpose of influencing unfavorably the growth of the ringworm fungus. Three per cent was selected because it was regarded as efficient and nonirritating. It is believed that the iodine in the combination described is in such a form that the iodine molecule becomes activated through photodynamic action and that its activity as a fungicidal agent is enhanced. In this series of 60 patients with tinea capitis 27, or 45 per cent, were cured, and such cures were determined by negative observations both by three successive direct examinations and by three inspections of the scalp hair with filtered ultraviolet rays.

#### SUMMARY AND CONCLUSIONS

A new topical application for tinea capitis is here proposed. In my hands it has cured 27 (45 per cent) of a series of 60 patients with ringworm of the scalp on whom this method of treatment was tested. In view of the almost epidemic proportions of tinea capitis at present, this local treatment appears to me worthy of trial, particularly since added experience has raised the proportions of cures to almost 70 per cent.

Dr. Lawrence Smith supplied the chlorophyll solution used in this study, and Miss Esther Liesner, technician at the Skin and Cancer hospital, made all the direct examinations.

The iodine preparation used for this work was donated by the Hersch-Razel Research Foundation.

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# TREATMENT OF TINEA CAPITIS WITH ROENTGEN RAYS

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**T**HE present epidemic of tinea capitis in New York city has offered opportunities to study the various methods of treating this disease and, in particular, the different procedures for epilating the scalp with roentgen rays. At the time of writing, we understand that the epidemic is nationwide. Our authority for this statement is from personal communications with dermatologists in different sections of the country. No one knows the exact number of cases of ringworm of the scalp in New York city, but estimates run in the neighborhood of 5,000. A vast amount of clinical material is essential to corroborate physical measurements and mathematical calculations. American dermatologists have been using for many years the Adamson-Kienboeck five point method for epilating the scalp, with uniform success. In various dermatologic centers, notably in Europe and Australia, experts advocate technics utilizing three, four, five and even seven focal points. The four point method of epilation of the scalp is the one preferred by Molesworth and Riddle<sup>1</sup> and by Schreus and Proppe<sup>2</sup>.

Molesworth and Riddle performed experiments to discover the correct focus-skin distances for the irradiation of heads of different sizes. Their mathematical calculations, based on the law of inverse squares, show that the use of any focus-skin distance greater than 8.5 cm. will cause an overdose in the region of the overlap. They stated that only infinite distance will provide complete overlapping. Adamson<sup>3</sup> recom-

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From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University.

1 Molesworth, E. H., and Riddle, A. R. The Effect of the Angle of Incidence upon the Dose of X-Rays Absorbed by the Skin, *Brit. J. Dermat.* **47**: 152 (April) 1935.

2 Schreus, H. T., and Proppe, A. X-Ray Epilation of the Scalp, *Brit. J. Dermat.* **48**: 113 (March) 1936.

*(Footnotes continued on next page)*

mended a distance of 16.5 cm and MacKee<sup>4</sup> a distance of 20 cm. These distances are a little more than half the correct distance (31.7 cm) as mathematically calculated by Bailey<sup>5</sup> for a hemisphere with a circumference of 48 cm.

When the scalp is irradiated for tinea capitis with the five point method of Adamson-Kienboeck, the areas between the centers of irradiation receive amounts of roentgen rays far in excess of those applied to the actual centers, according to Molesworth and Riddle. The increased dose in the overlapped areas is dependent on the focus-skin distance. Shanks<sup>6</sup> observed that in cases in which the hair failed to grow after roentgen ray epilation the centers of irradiation always escaped (chart 1A). Permanent depilation was noted only in the parietal areas. Molesworth and Riddle advocated the four point system of irradiating the scalp so that the disparity of distribution of dosage could be reduced and the margin of safety made wide enough to permit the performance of roentgen ray epilation with almost complete safety in all cases. It has

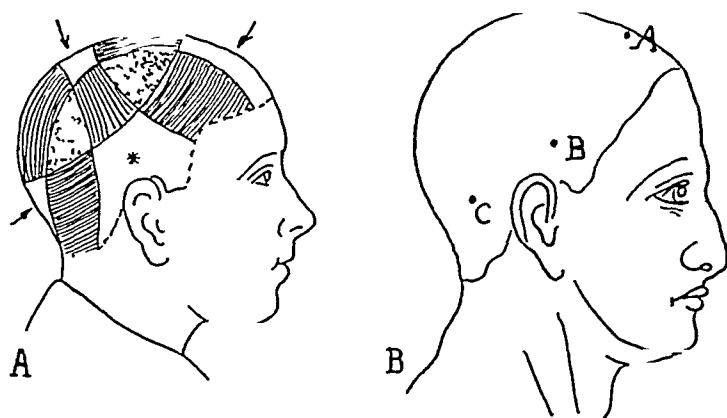


Chart 1—A, overlapping from three focal points in the anterior and posterior parietal areas when the Adamson-Kienboeck technic is employed (From Schreus and Proppe<sup>2</sup>) B, focal points of irradiation when Epstein's technic is employed. The five points are along the crown of the scalp. The vertex is not irradiated. The occipital region is irradiated from both the right and the left side (From Epstein<sup>7</sup>).

been conclusively proved and the findings were corroborated that in the five point method of scalp epilation a greater dose is applied to the areas of overlap than to the focal centers. It is therefore obvious that the margin between the smallest dose that will cause epilation and the largest

3 Adamson, H. G. A Simplified Method of X-Ray Application for the Cure of Ringworm of the Scalp. Kienboeck's Method, *Lancet* **1** 1378 (May 15) 1909.

4 MacKee, G. M. X-Rays and Radium in the Treatment of Diseases of the Skin, ed. 3, Philadelphia, Lea & Febiger, 1938.

5 Bailey, V. A., cited by Molesworth and Riddle<sup>1</sup>.

6 Shanks, S. C. X-Ray of Ringworm of the Scalp. A Survey of 2,400 Cases, *Brit. J. Dermat.* **43** 477 (Oct.) 1931.

dose that will just fail to prevent regrowth must be much greater than had been thought

Molesworth and Riddle objected to the five point method and suggested a four point method of scalp epilation which eliminates the exposure of the vertex. A detailed description of the four point method is not given.

According to calculations, the dose applied to the overlap region was almost twice that applied to the focal areas when the five point method of Adamson and Kienboeck for epilating the scalp is employed. We corroborated this finding by actual iontometric measurements. It is therefore difficult to understand why more patients with permanent epilation are not observed. This aroused great interest and discussion.

In 1936 Epstein<sup>7</sup> corroborated the findings of Molesworth and Riddle in regard to the amount of radiation which the scalp can tolerate, and he cited an example in which a single area of the scalp had received 540 r without ill effect. Their epilating dose was 300 r. This clinical observation verified the fact that almost twice the epilating dose may be applied to an area of the scalp without causing permanent alopecia. At the Universitatshautklinik, Breslau, Epstein did not employ the Adamson-Kienboeck method. Instead he epilated the scalp by exposing the following five fields (chart 1 B).

Field 1 scalp from above, point of adjustment in the median line about 3 to 4 cm behind the forehead hair line

Field 2—right temple, point of adjustment about 3 cm above the upper rim of the ear

Field 3—left temple, point of adjustment corresponding to field 2

Field 4 right occiput, point of adjustment about 3 cm above the nape hair line, the ray of incidence goes through the vertical axis of the skull and forms, with a sagittal plane, an angle of 45 degrees

Field 5—left occiput, point of adjustment corresponding to field 4

It can thus be seen that in Epstein's method five irradiated areas are situated along the circumference of the scalp, and the only radiation reaching the whorl is by overlap. Measurements were made with the Hammett Dosimeter, and the number of roentgens for each exposure used for children up to 4 years of age amounted to 240, in older children a dose of 270 r was given. The apparatus used was a condenser in a Villard connection, a Metallix tube in a shock-proof hood delivering 100 kilovolts, 4 milliamperes, filtered through a glass cylinder equivalent to 0.5 mm of aluminum and with a focus-skin distance of 30 cm. The

<sup>7</sup> Epstein, S. The Importance of Overlapping in Irradiation of the Scalp, *Brit. J. Dermat.* **48**: 1 (Jan.) 1936



diameter of the field was 20 cm and the intensity rate 35 r per minute. Measurements were made in the overlapped areas, and it was seen that even though 240 r was applied to each focal point the overlapped areas received a combined dose of nearly 500 r.

There are several objections to Epstein's method. The danger of overirradiation in the overlapped regions is accentuated. Different doses are applied to children of different ages, and different measurements are used for scalps of different sizes. This introduces two variables which may lead to error. Doses and measurements should be fixed.

We fully agree with the statement of Schreus and Proppe that roentgen ray epilation of the head is one of the most difficult performances in roentgen ray therapy. They have expressed themselves as definitely against the use of the five point Adamson-Kienboeck method of scalp epilation and as favoring four point method for the following reasons: 1. The dose is uniformly distributed over the entire scalp. 2. The areas between the centers of irradiation are not overdosed. 3. The epilation produced by the five point method is not more uniform than that produced by the four point method, but with the five point method the possibility of subsequent damage is greater.

In studying the exact technic advocated by Schreus and Proppe, one is confronted with the vagueness of the description of the technic. In fact, it has been impossible to find in any writings at our disposal an exact explanation of how to mark off the scalp prior to irradiation. Schreus and Proppe roughly indicated that one point is in the occipital area just below the protuberance, the second point is somewhere in the region of the anterior fontanel, and the lateral points are somewhere in the parietal areas, just above the ears. These points vary with the size and shape of the head, and an experienced operator would have difficulty in carefully plotting out the scalp prior to irradiation. In addition to the inaccurate plotting of the scalp, a dose of 400 r is recommended for each focal point with 110 kilovolts and a filter of 0.5 mm of aluminum. The roentgen measurements were made with the Mekapion Dosimeter.

We have been working on this problem for over a year, and we have found it difficult successfully to epilate the scalps of children according to the vague method of Schreus and Proppe.

The early failures obtained with the four point method of irradiating the scalp stimulated us to investigate the causes of failure and to devise a simple four point method. Our four point method of irradiating the scalp evolves about a single point in the direct center of the scalp. A line is drawn from the anterior to the posterior hair line in the sagittal plane. The distance is divided in half and marked with a skin pencil. Perpendicular to this line at the center mark, another one is drawn

running from ear to ear. The point at which they cross is the exact center of the scalp.

The patient is now placed on a table in the supine position and the head rotated 90 degrees to the right, exposing the left parietal area. To expose the right parietal area, the head is turned to the left. The frontal area is exposed by simple flexion of the head with the aid of pillows or sandbags, so that the chin rests comfortably on the chest. The occipital area is exposed by placing the patient on the table in the prone position. Pillows are placed under the chest, with the forehead resting on the table.

In order to obtain the correct position, angle and distance of the tube in relation to the patient, two simple devices are essential. One is a measuring or centering rod which measures the focus-skin distance of 25 cm. This rod is attached at one end to a diaphragm which fits in the filter slot of the protective box. A mark is placed at the center of the measuring rod (12.5 cm from the skin surface). The other device is a long tongue depressor.

The tube, with the centering rod in position, is placed over the left parietal area in such a way that the pointer lines up with the line which runs from ear to ear. Now one end of the tongue depressor is pressed with the index finger against the central point of the scalp. The other end of the tongue depressor points toward the 12.5 cm mark on the measuring rod. The tube is now tilted so that the halfway mark on the pointer and the tongue depressor meet. This determines the exact angle at which the tube is to be tilted, the exact distance between the skin surface and the target, the exact area of the scalp to be irradiated and the distance from the central point. When the tube is set, the pointer must still be lined up with the parietal line and must point perpendicular to the scalp. The ear is bent over and held in place with adhesive tape. The ear and the remaining glabrous skin are protected with lead foil or lead rubber. A dose of 300 r measured in air with a Victoreen meter is administered. The kilovoltage may be from 60 to 100, no filter is used and the focal skin distance, as previously mentioned, is 25 cm. The process is repeated for the right parietal area, then for the frontal and finally for the occipital area. The five accompanying diagrams simplify the foregoing verbal explanations. The technic is simple when actually carried out (charts 2 and 3).

Using this method, we treated over 75 patients with tinea capitis caused by *Microsporon audouinii*. In most patients the epilations were perfect. In a few instances in which the heads were large or disproportioned, some hair failed to come out from the preauricular regions, from the nape of the neck and from about 1 cm of the anterior hair line. The results on the whole were satisfactory. Practically all

patients treated were cured in four to eight weeks after the epilating dose was applied. It should not be necessary to emphasize the importance of using an adhesive cap and to proceed with appropriate postepilation treatment to assure success.

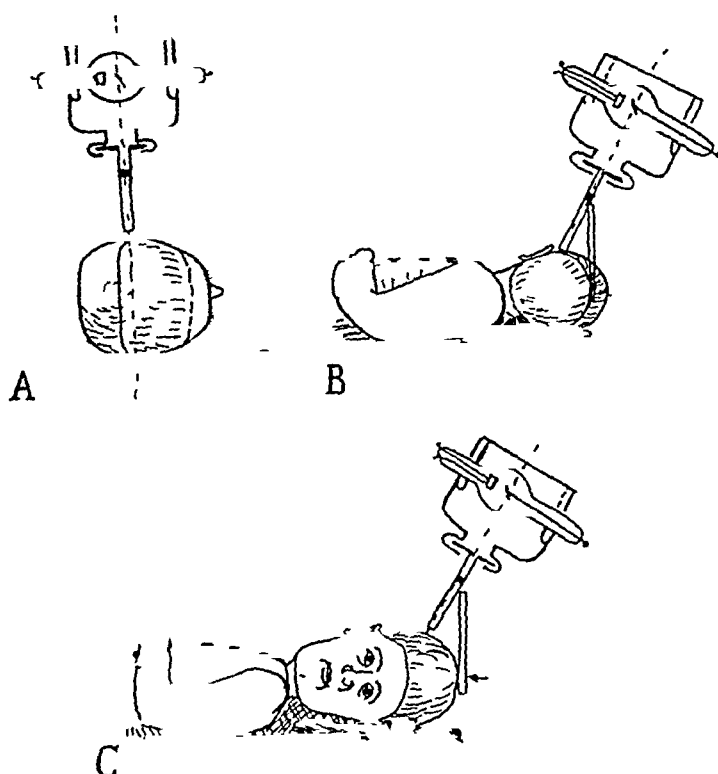


Chart 2—*A*, position of the tube in relation to the scalp when the four point method of irradiation is employed. *B*, position of the head for irradiation of the left parietal area. Note correct angulation of the tube and the relationship of the centering rod to the tangent, which goes through the central point of the scalp. Note the same features in *C* and in chart 3. *C*, position of the head for irradiation of the right parietal area.

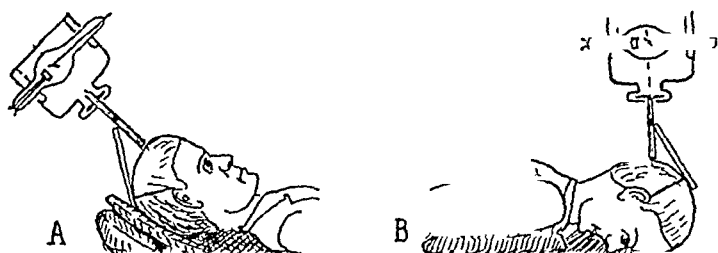


Chart 3—*A*, position of the head for irradiation of the frontal area. *B*, position of the head for irradiation of the occipital area.

The advantages of the four point method just described are simplicity of application, saving of time, making unnecessary the application of an epilating dose to a difficult area—the vertex—and, most important, elimination of the danger of overirradiation in the parietal areas when the five point Adamson-Kienboeck technic is employed.

The five point Adamson-Kienboeck technic of scalp epilation is so well known and so well explained in standard textbooks that a description of it is not necessary. However, it is advisable to make some comparisons between the five point Adamson-Kienboeck technic of scalp epilation and the other methods described in this paper. The Adamson-Kienboeck method probably is used oftener and has been used longer and under more varied conditions than any other method. This is proof that it has stood the test of time. It is conceded that instances of permanent epilation have been noted. It is our opinion that this has not been the fault of the technic but that the causes are probably found in faulty apparatus, improperly calibrated apparatus or faulty manipulations. It is also conceded that the geometric and mathematical calculations prove that a dose of roentgen rays at the intermediary areas is much greater than that at the focal points. This amount of excess radiation is not sufficiently great to cause any damage. The factor of safety is evidently great, being more than twice the epilating dose. In the Adamson-Kienboeck technic it is necessary to irradiate five points, and the one on the vertex is somewhat difficult. This is a disadvantage but not a serious one.

We do not believe that the advantages claimed for the newer methods of scalp epilation and theoretic claims made against the Adamson-Kienboeck technic are sufficient to persuade one who is used to the method which has stood the test of time to give it up and adopt a new untried method. For routine scalp epilation the Adamson-Kienboeck technic is still the one of choice. It is safe and easy to use. Correct plotting of the scalp, proper calibration of the roentgen ray apparatus and careful linear and angular measurements are essential prerequisites to successful results, regardless of the method employed. We have employed the Adamson-Kienboeck technic of scalp epilation in over 1,000 cases during the past several years and found it to be satisfactory. In none of our patients have we observed either partial or complete permanent depilation.

As a result of studying the various methods of epilating the scalp in cases of tinea capitis, we are forced to the conclusion that there is no ideal way to epilate the scalp. This is due to difficulties arising from technic and other mechanical factors and also to difficulties encountered because of the great variations in the size and shape of scalps. In some the parietal regions protrude, in others the occipital protuberance is large. Some patients have flat heads, while others have pointed heads. The microcephalic and the hydrocephalic types make proper plotting of the scalp difficult. At the present writing we prefer as a routine method of epilating the scalp the five point method of Adamson-Kienboeck. This is probably due to the fact that we have long been familiar with

it The four point method as described in this paper is easy to apply and removes the objection of excessive exposure of the parietal areas

In the control of any epidemic it is necessary to devise short cuts to treatment Lewis and Hopper<sup>8</sup> have advocated the treatment of localized infected areas of the scalp with roentgen rays By treating a single infected area much time is saved The method is successful in some cases We have used this method for several years We do not advocate it, because the unsuccessful results have been too numerous In these cases with unsuccessful results it took from six months to one year to obtain a cure It is considered unsafe to apply a second epilating dose of roentgen rays in less than six months after the first one The failures are probably due to the fact that the infection probably starts on several areas of the skin of the scalp The hair on the scalp becomes infected later When examined with filtered ultraviolet rays (Wood's light), only infected hairs fluoresce An epilating dose of roentgen rays is given to the fluorescent area or areas, and while these treated areas are being cured other untreated areas start showing fluorescence We have had this experience repeatedly, even though we covered the known infected areas with adhesive tape and protected the supposedly uninvolved areas with protective ointments and antifungus agents We advocate now, as was advocated by the older dermatologists, complete epilation of the scalp in preference to epilating single areas for the treatment of tinea capitis caused by *M. audouinii*

#### CONCLUSIONS

1 There is a nationwide epidemic of ringworm of the scalp caused by *M. audouinii*

2 At some dermatologic centers in Europe and Australia, the three, the four, the five and even the seven focal points are employed for epilating the scalp with roentgen rays The more important methods are discussed

3 We describe in detail a four point method of epilation of the scalp However, we prefer for routine epilation the five point method of Adamson-Kienboeck because we believe it to be simple and safe and because it has stood the test of time

4 We do not favor the method of epilating individual infected areas with roentgen rays because our percentage of failures has been too high

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<sup>8</sup> Lewis, G. M., and Hopper, M. E. Ringworm of Scalp, *Arch. Dermat. & Syph.* **49**:107 (Feb.) 1944

## ABSTRACT OF DISCUSSION

DR GEORGE M LEWIS, New York The present epidemic has focused attention on this disease and has shown the importance of adequate prophylactic and therapeutic measures From my information, there are thousands of cases in various cities throughout the United States

In the management of the epidemic, public health measures are essential A practical plan was evolved in a recent paper (*N Y State J Med* **44** 1327 [June 15] 1944)

From the individual dermatologist's standpoint, the type of therapy that should be used en masse is of great importance My colleagues and I have tried various of the newer fungicides and have employed some of the newer penetrating bases Partial success is obtainable, but reliance on any therapy involving local medication has not yet proved practical in our hands when the infecting micro-organism was *M. audouinii* For this reason, I subscribe heartily to what Dr Cipollaro said about the treatment of tinea capitis I believe at this time that roentgen ray therapy is the treatment which should be employed in the majority of cases, and I believe that the only exceptions are cases of very young or feebleminded children or those used for experimental study

At New York Hospital, we employ the five point method of roentgen epilation, except that when a child (particularly a girl) has a small area of infection we feel that it is well worth while to attempt treatment by spot roentgen ray epilation From our published report (*Arch Dermat & Syph* **49** 107 [Feb] 1944), I wish to modify in only a slight degree the technic The scalp is shaved on and around the patch The child is carefully inspected under filtered ultraviolet rays for other areas of infection No roentgen rays are administered for at least two weeks, during which time the results of culture become known During these two or more weeks, grease containing 5 per cent ammoniated mercury is applied all over the scalp No shampoo is allowed until the day set for roentgen ray epilation The scalp is then inspected under the filtered ultraviolet rays If there are no new areas of infection, the epilating dose of roentgen rays is given, 10 per cent greater than the dose used with the five point method After the epilating dose of roentgen rays, we reapply 5 per cent ammoniated mercury ointment to the area and to the entire scalp We do not wash the scalp We have the mother reapply the salve each day After three weeks, when the hair begins to loosen, the mother is told to shampoo the hair thoroughly and to have the child report to us We apply adhesive tape and remove the rest of the infected hair

The question of keeping infected children at school or of excluding them from school is of practical importance Dr Peck, I know, believes that they should stay in school, and I believe that they should not My reasons are (1) difficulty of segregation, (2) mixing of hats, (3) irresponsibility of youth and (4) placing of parents' responsibility on school authorities

DR GEORGE C ANDREWS, New York There is nothing especially new about these different methods In 1921 there was an epidemic of ringworm of the scalp caused by *M. audouinii* in Hamburg, Germany, and I read of the experiences at that time, which were reported in the *Dermatologische Wochenschrift* The seven point, the four point and the three point methods were being used for epilation of the scalp in England and in Germany back in the 1920's The Adamson-Kienboeck five point method has stood the test of time I know that I personally have used it ever since it was taught to me by Dr Remer and Dr MacKee in 1919 I estimate that during this interval I have epilated

between four and five thousand children for ringworm of the scalp I have never during that time seen a patient with permanent partial or complete epilation, that is, I have never seen a patient in whom there was any undesirable permanent effect

At the Vanderbilt Clinic during the past ten years, over 2,000 scalps have been epilated During the present epidemic, my colleagues and I are epilating 6 to 8 patients a day, and that has been the average for nearly a year Our epilations are more uniform than they used to be with the old type of equipment We are using 400 r as the epilating dose That is the dose that Braestrup and I recommended in 1935, and we are using 60 kilovolts as voltage and the five field method I still advocate that dose

Of course, the dose of 300 r suggested in Dr Cipollaro's paper may produce epilation There are different degrees of epilation According to Hallem in the *British Journal of Dermatology*, there is a 25 per cent latitude in the epilating dose I believe that the latitude is much greater than that That is pretty well established, because if one gives 400 r to the focal point on the scalp, owing to overlapping one gets around 550 to 600 r in the intervening areas, and with perfect safety If, for instance, the New York Post-Graduate Medical School and Hospital uses 300 r and the Vanderbilt Clinic uses 400 r, there is a latitude of 25 per cent, an amount which is within safe limits

I believe that roentgen ray therapy is the most efficient method of treatment and that the one field method epilating only the diseased spot is not advisable because of the uniform success of the five field method I also believe that if one area is epilated successfully and then the infection spreads to the rest of the scalp, as I believe Dr Lewis said occurred in about 25 per cent of the cases at New York Hospital, one is faced with the problem of what is to be done with the patient, because he is not cured and one area has been epilated Should it be epilated again? It might be safe to do that within a few months, but after just how long an interval is always a question One does not like to hold up the cure for two or three months in order to epilate again

I might say that in 1921 when this epidemic was in progress in Hamburg I went to Dr Shirley Wynne, who was then Commissioner of Health in New York city, and told him what I thought of the danger of an epidemic in New York city I said that I thought the precautions then taken were extremely lax and should be changed since the only regulation about school children then was that they had to be under the care of a recognized physician or clinic in order to attend school He told me that the health department was not interested in ringworm of the scalp since the disease never had caused them any trouble, but he said that they were interested in pediculosis of the scalp and that if I had some suggestions to make regarding it he would like to know about them I told him that the two diseases were somewhat similar, that no changing of hats among the children and the keeping of hats on separate hooks were especially important, but I did not accomplish anything with Dr Wynne

DR SAMUEL M PFICK, Bethesda, Md The Dermatoses Section of the United States Public Health Service has been consulted by a number of communities to aid them in controlling the epidemic of ringworm of the scalp While no one denies that roentgen ray epilation is the most successful single treatment for this disease, it is an impractical procedure when thousands of patients are to be treated This is especially true when one realizes that many communities with populations of twenty or thirty thousand have no facilities for roentgen ray epilation, even if it were possible to carry out this procedure on a large scale In our recommendations we do not propose to keep infected children away from school

nor do we propose that separate schools or classes be set up solely for their use. Even if such segregation were practiced as far as schools are concerned, it certainly would not prevent contact between healthy and infected children outside the school rooms. Segregation would have to be practiced in the Sunday schools, in the movies, in the playgrounds and even in the homes. Every one admits that such a plan is impossible to carry out. For this reason, the Dermatoses Section proposes that instead of segregation of the infected children they be allowed to attend school under certain conditions. These conditions consist of (1) the wearing of properly made head coverings by all children in school, (2) the routine use of the Wood filter at frequent intervals to locate infected persons, (3) the establishment of treatment centers in the schools, if possible, for the infected children, (4) close clipping or depilation of the hair of the infected children, (5) the use of antiseptic ointments by the infected children, (6) proper regulation of barber shops to prevent spread of the infection, (7) instruction of parents to prevent infection and reinfection, and (8) the use of roentgen ray epilation when feasible.

DR CARROLL S. WRIGHT, Philadelphia. I should like to ask one question. I was unfortunate enough to be selected by the Director of Health of Philadelphia to look after the epidemic there. Dr. Peck knows this, as he came as a representative of the United States Public Health Service to discuss the problem with us.

Temple University School of Medicine does not have an x-ray department in the section of dermatology. The work is all under the department of roentgenology, headed by Dr. Edward Chamberlain. I asked him if he would be willing to epilate the few patients we had at our clinic, and he refused on this ground. He thinks that there is great danger of damaging the pituitary glands.

I should like to ask whether any one has any information on this subject or can answer the question as to the possibility of pituitary damage from roentgen ray crossfire.

DR CHARLES C. DENNIE, Kansas City, Mo. I should like to ask a couple of questions about this, since it is admitted that epilation does not, of course, kill the fungus. I think that it is most important to know what the after-treatment of these patients is, and, second, if this epidemic is spread by the electric clippers or any other kind of clippers what method of procedure barbers should use to sterilize these instruments, in which it is known that the fungus is hard to kill. These two questions I should like to have answered.

DR C. GUY LANE, Boston. Since the last war, we have had an excellent cooperative arrangement at the Massachusetts General Hospital between the dermatologic department and the x-ray department so that we have had the apparatus and technicians there for one morning a week. During that time my colleagues and I, with the cooperation of the roentgenologists, have had charge of epilations. It has worked out well during that time.

We have noticed, as Dr. Cipollaro has stated, that there is frequently more epilation over the anterior parietal area on each side than anywhere else. I have considered the idea of using a four point method, and I shall go back with the idea of treating some patients by that method.

To compensate for that anterior parietal baldness, I have roughly indicated to the residents that, instead of having the stick which measures the target-skin distance exactly perpendicular to the tangent at the site to be treated, they should have the stick tipped back a little, so that there is an acute angle rather than an exact right angle on the occipital side of the stick as it contacts the scalp.



Another observation is that it is not always necessary to get 100 per cent epilation in order to obtain a cure. We have aimed rather, perhaps, at 80 to 90 per cent or, roughly, at 90 per cent. It has always seemed better to me to see a few hairs left on the head twenty-one days after epilation than it is to see a completely bald scalp.

I have also been impressed in a few instances with what I feel is the narrow margin of a minimum epilating dose. In a few patients in whom the nuchal depression in the back of the neck has been rather deep, we have noticed hairs still growing when the ridges on either side have been perfectly smooth and bald. In other words, the distance of a few millimeters apparently makes a difference between epilation and nonepilation, and that is, of course, noted in the occiput at times, where there is a center area of baldness and the surrounding hair is still present. It is also well for the person doing the treatment to indicate that particular area with adhesive tape or red ink in order to be sure that area is not treated again. An experience earlier, when the same area was treated twice, has emphasized this precaution.

DR F J EICHENLAUB, Washington, D C. There has also been one difficult question for me in these discussions of roentgen ray dosage. Dr Cipollaro says 300 roentgen units, and Dr Andrews says 400.

I did have two machines in my office, one in one room and one in another, both of which I used for unfiltered radiation. One epilated with 275 r and the other with 400 r.

I wonder if we might not go back a little bit more to the biologic consideration of roentgen ray dosage and speak of it a little more accurately. Certainly, the roentgen unit measurement of unfiltered radiation is variable.

DR JOSEPH GRINDON, St Louis. May I ask a question? What is Dr Lane's minimum epilating dose?

DR C GUY LANE, Boston. My minimum epilating dose is 300 r, measured by the Victoreen meter. My co-workers and I worked up gradually to the 300 r, when we started measuring with the Victoreen meter.

As time went on, we found that we had a series of 10 or 15 cases in which we got 100 per cent epilation. Since that time we have reduced our dosage to 290 r of unfiltered rays, then to 280 r and then to 270 r. We have our output measured every day that we use the machine for treatment. We plan to obtain, as I say, 80 to 90 per cent epilation.

DR EDWARD A OLIVER, Chicago. While dermatologists in Chicago have not treated nearly so many patients as those in New York, we have had excellent results using a dosage of only 275 to 300 r. Our percentage of cures is 96.3, and 3.7 per cent of the patients required further treatment.

The point that has not so far been mentioned is the use of the Wood filter. We find it difficult to tell anything about the progress of the disease without examining every patient with the Wood light.

Time and again we have had patients in the clinic and in the office with lesions barely perceptible to the eye, but when we took them into the dark room and examined them with the Wood lamp we found the scalp full of infection. I think it should be an essential part of every dermatologist's equipment.

DR LAWRENCE G BEINHAUER, Pittsburgh. Since the question of the Wood light has been brought up, we found that during the recent epidemic in Pittsburgh we were unable to obtain a sufficient number of Wood filters to pass on to the general practitioners. We found, however, a most convenient substitute for the Wood lamp, which can be obtained for the price of \$1.25. It is the 250 watt

Purple X Lamp made by Westinghouse It has a life of fifty hours If it is used intermittently and burned no longer than a minute—because the glass becomes soft—one can check patients efficiently The only difference between this bulb and the regular Wood lamp is the concentration of light We have checked it with the Wood lamp in about 350 cases and found it convenient for use in the office It may be used in the ordinary standard stand, with the bulb directed down on the scalp It is efficient, and I recommend it

DR ANTHONY C CIPPOLARO, New York It is difficult to cover all points that have come up in the discussion

The reason for discussing the four point method of epilation of the scalp is that some writers in Europe have assigned definite benefits to this method We therefore found it necessary to epilate the scalps of children suffering with *tinea capitis* by means of different methods so that we could compare their advantages and disadvantages

I agree with Dr Lewis that patients with ringworm infection of the scalp should be isolated Experience has already proved in the European epidemics that the combination of isolation plus roentgen ray epilation brought an end to the epidemics At the present time there is no better way of treating *tinea capitis* caused by *M. audouinii* All the topical remedies so far used have given poor results compared with those obtained with roentgen ray epilation

I should like to spend a few minutes on Dr Andrews' and Dr Eichenlaub's discussions regarding the number of roentgens required to produce epilation There is a direct relationship between the biologic effect and the number of roentgens required to obtain such biologic effect Some iontoquantimeters give one reading for a given biologic effect and others give entirely different readings Commercial iontoquantimeters also vary with the mean wavelengths of a roentgen ray beam Iontoquantimeters should be calibrated against an open standard chamber and against a biologic effect, such as erythema or epilation I hope that I have made clear that there is no uniformity in the readings of different iontoquantimeters This is the basic reason that one dermatologist requires 400 r for an epilation and another requires 300 r for the same biologic effect If the same iontoquantimeter were used to calibrate the two roentgen ray machines, the number of roentgens would be the same As an additional safety factor, all x-ray machines should be calibrated against a biologic standard, viz, the erythema dose or the epilating dose With our iontoquantimeters, we measure the epilating dose to be 300 r This amount of radiation gives us complete epilation in every case

Dr Wright brought up the question of danger to the pituitary glands and other intracranial structures when the scalp is epilated with roentgen rays I do not believe that any harm to the brain or to the pituitary gland can result when the entire scalp is irradiated for ringworm and when low voltage unfiltered roentgen rays, as commonly employed by dermatologists, are used There may be danger if one employs high voltage heavily filtered roentgen rays

# JUXTA-ARTICULAR NODE OF LEPROUS ORIGIN

H PORTUGAL, M D  
AND  
GLYNNE L ROCHA, M D  
RIO de JANEIRO, BRAZIL

**J**UXTA-ARTICULAR nodes are now regarded as a syndrome. In the first cases reported by A Lutz<sup>1</sup> and E Jeanselme,<sup>2</sup> the cause was syphilis, and this is the cause in the great majority of cases observed over nearly the whole world, though some other diseases can present this manifestation. Van Dijke and Oudendal,<sup>3</sup> Clapier,<sup>4</sup> Van Loon,<sup>4</sup> Genner<sup>5</sup> and others have shown the part played by yaws, while Jeanselme<sup>6</sup> and I de Jong, Bruenauer<sup>7</sup> and Gadrat and Salvador<sup>8</sup> have demonstrated tuberculosis as the cause. The part played by leprosy, although suspected by F Wise,<sup>9</sup> has not up to now been proved beyond doubt. This case which we are reporting shows definitely that *Microbacterium leprae* can produce juxta-articular nodes.

## REPORT OF A CASE

P A das S, aged 61, was a white married Brazilian policeman. His family history was not significant. His personal history revealed that he had had gonorr-

From the Clinic of Dermatology and Syphilology, The University of Brasil, Prof F E Rabelo

1 Lutz, A. Brief aus Honolulu, September 1891, *Monatsh f prakt Dermat* **13** 389 and 488, 1891

2 Jeanselme, E. Les nodosités juxta-articulaires, in *Traite de la syphilis*, Paris, Gaston Doin & Cie, 1932, vol 3

3 Van Dijke, M J, and Oudendal, A F J. Distribution, Histology, Etiology of the "Nodosités Juxta-Articulaires" (Juxta-Articular Nodules Jeanselme) Among Malay People, in *Reprints from the Reports of the Dutch-Indian Medical Service*, 1923, vol 2, p 143

4 Cited by Burnier, R. Les nodosités juxta-articulaires et leurs rapports avec la syphilis, *Presse med* **41** 995, 1933

5 Genner, V. Sur l'étiologie des nodosités juxta-articulaires, *Ann de dermat et syph* **6** 675, 1925

6 Jeanselme, E. A propos du procès verbal, *Bull Soc franç de dermat et syph* **41** 859, 1934

7 Bruenauer. Ueber multiple fibromatose, kutan, sub-kutan Knoetchenbildungen ueber und in der naeche von groesseren und kleineren Gelenken, in *Congrès international de dermatologies et de syphilographie*, Copenhagen, 1931, p 738

8 Gadrat, J, and Salvador. Nodosités juxta-articulaires et tuberculose, *Bull Soc franç de dermat et syph* **41** 669, 1934

9 Wise, F. Leprosy with Juxta-Articular Nodules, *Arch Dermat & Syph* **41** 789 (April) 1940, **42**:1162 (Dec) 1940

rhea and that twice he had noticed an ulcerative lesion on the penis (presumably chancroid) many years ago

The first symptoms of leprosy appeared eleven years before he consulted us as pigmented patches on the arms and forearms. Believing that he had syphilis, the patient took injections of neoarsphenamine and a bismuth preparation, but his condition grew worse. In 1935 leprosy was diagnosed, and the patient submitted to an eclectic treatment, which left several small whitish scars, shown in figure 1. He was registered on Dec. 14, 1939 in the service of leprosy, by Dr. H. Caldas. At that time he had, besides the spots on the arms, inflammatory nodules scattered



Fig. 1—Leprotic juxta-articular node. The whitish small scars are effects of the physical therapy.

over the body (leprous reaction). Two years before we saw him a hard nodule appeared near the right elbow. The patient did not worry about this lesion, as it did not cause any trouble. We found it during a clinical examination on July 19, 1944.

The patient is short and robust, with well developed subcutaneous fatty tissue. There are numerous small whitish scars on the face, arms and forearms, resulting from the galvanocautery therapy. On the forearms, arms and thighs are large yellowish infiltrated patches, which are folded with difficulty. Near the upper apophysis of the right ulna there is a nodule the size of a chestnut. Although

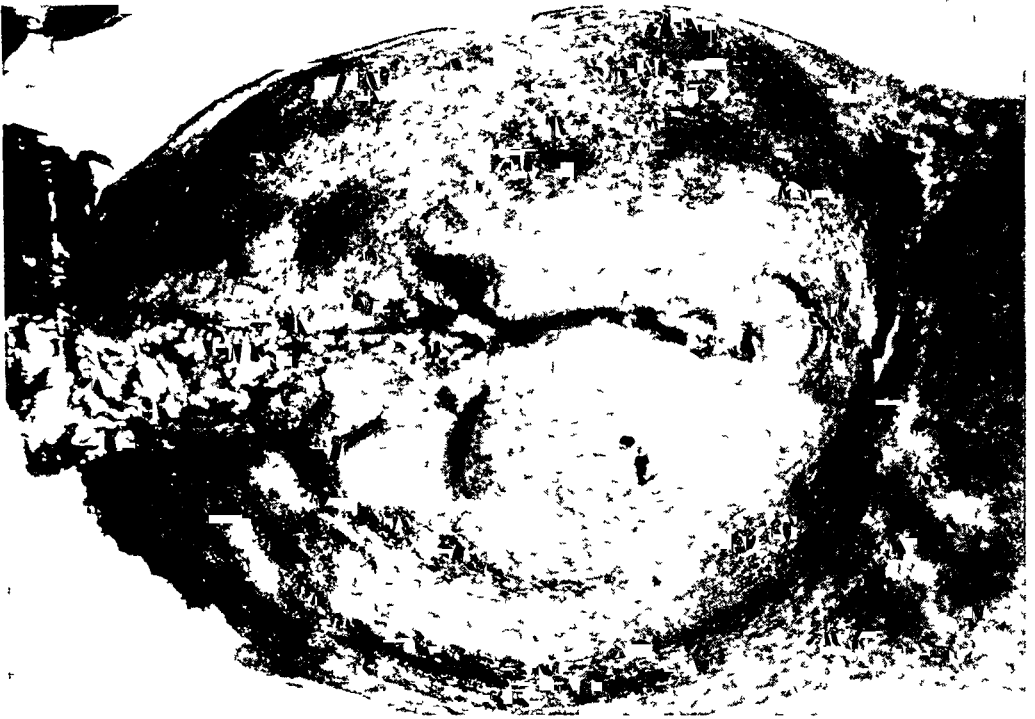


Fig 2—Microscopic aspect of a lobe ( $\times 30$ ) of a leprotic juxta-articular node

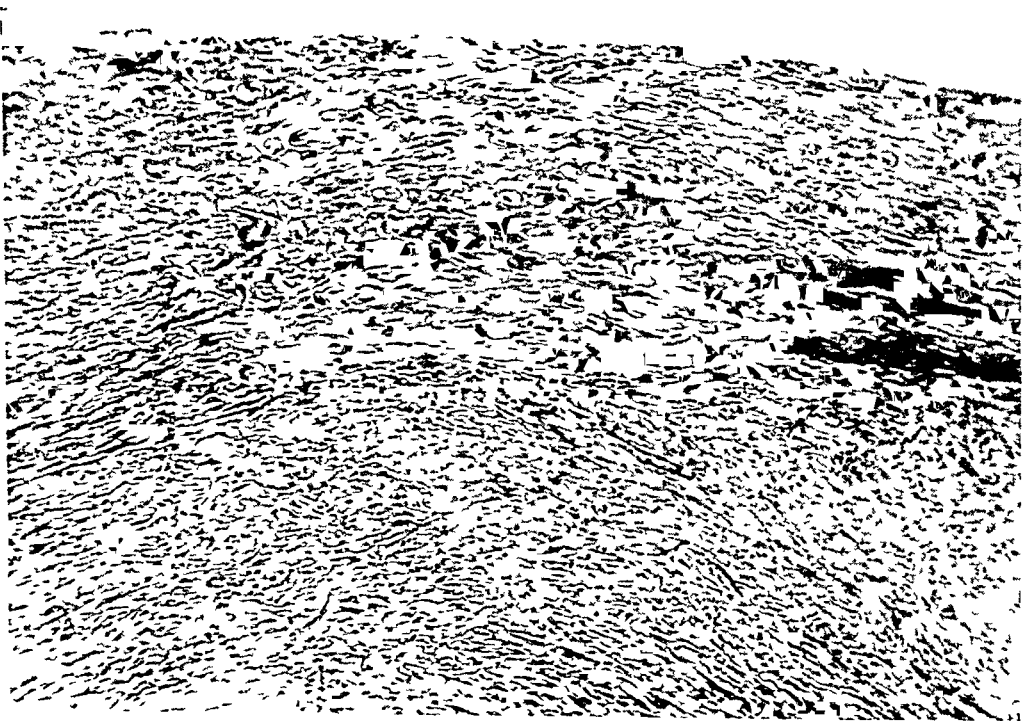


Fig 3—The marginal zone, the peripheric fibrous tissue with numerous capillaries and small cellular infiltrates and the leprotic granuloma ( $\times 200$ ) of a leprotic juxta-articular node

the thick infiltration of the skin makes palpation difficult, its hardness can be perceived. There are no similar lesions near the other joints.

The Wassermann and Kahn reactions were negative. The examination of the internal organs revealed an increase of the aortic arch.

The nodular lesion was removed under local anesthesia (ethyl chloride). It was a whitish nodule of ellipsoid shape, measuring 3.2 by 2.9 by 1.3 cm. It was uniformly hard. In transverse section the surface was white and homogeneous at the periphery and yellowish at the center, where it was divided into compartments by septums starting at the periphery. An irregular crack ran in the direction of the transverse diameter from one side almost, but not quite, to the other, this gave the impression that the nodule was a thick layer folded over.

The histopathologic examination showed that the peripheral zone consisted of fibrous tissue which, in the form of septums, penetrated into the interior of the

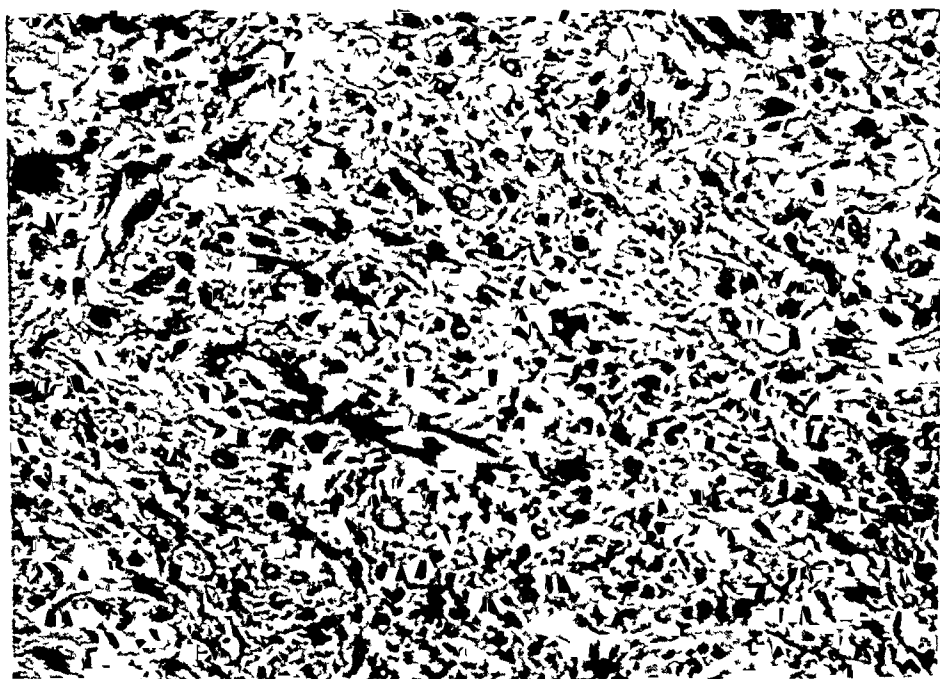


Fig. 4—Central zone, with numerous "lepra cells of Virchow" ( $\times 450$ ) of a leprotic juxta-articular node.

nodule, marking off lobes of various size. In most of these lobes there could be distinguished the three zones described by Jeanselme.<sup>2</sup> The outer zone consisted of collagenous fibers running tangentially to the nodes, these fibers were separated by capillaries and infiltrated pericapillaries. The median zone was occupied by veritable skeins of neocapillaries and infiltrated histiocytes, the collagenous fibers were separated by intense edema. The central zone, the largest of all, consisted of clear vacuolated cells, with a well defined nucleus, containing drops of single refracting material, stained orange by scarlet red, there were also numerous acid-resistant bacilli. The lesion had, therefore, the typical structure of a leproma. In some of the smaller lobes only an inner and an outer zone could be distinguished, the former consisting of fusiform slightly vacuolated cells.

From the description the case is one of juxta-articular node in a patient suffering from leprosy. The cause of the lesion cannot be doubted, owing to the presence of Virchow cells and acid-resistant bacilli in the interior of the node. Therefore, the hypothesis of an association of juxta-articular nodes of another origin with leprosy is out of the question. The leprotic juxta-articular node does not appear to have any especial clinical feature. Nodes of syphilitic origin are generally multiple, in our case there was a single node. However, solitary nodes in syphilis were observed by Jeanselme, Burnier and

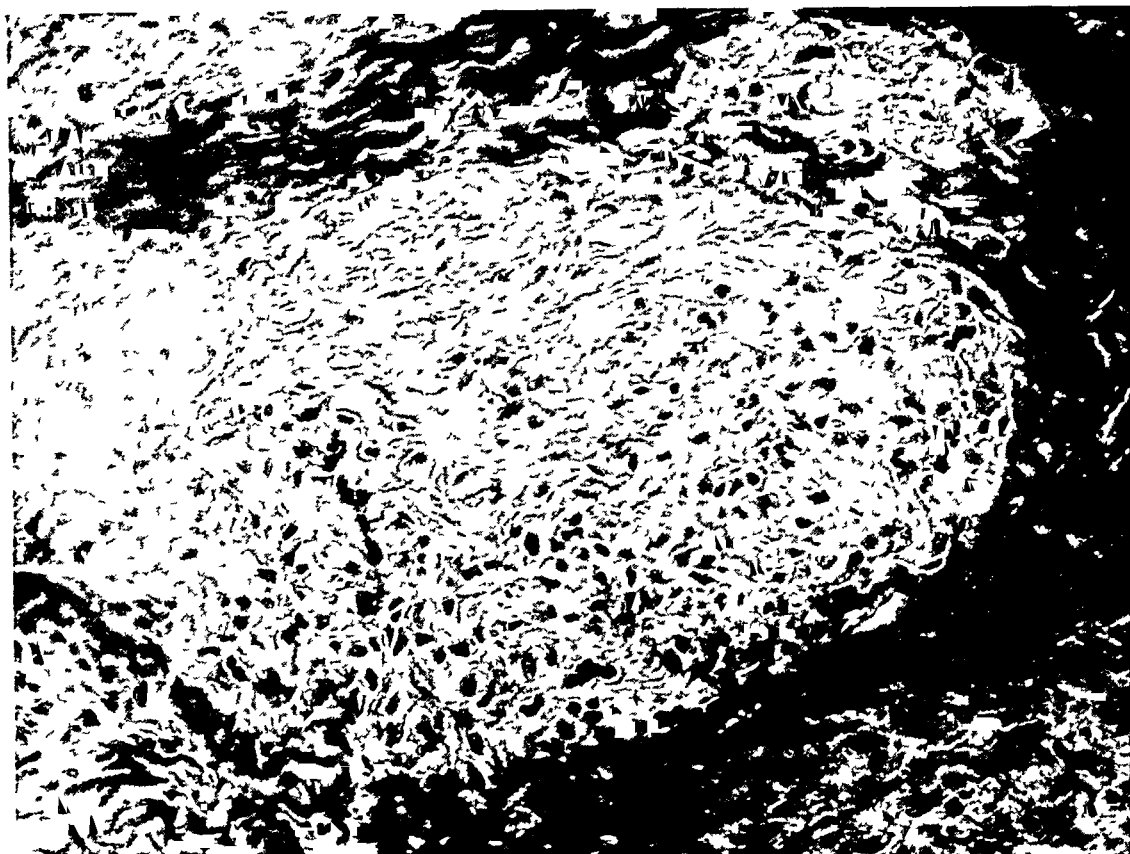


Fig 5—Fibrous tissue, without intermediary zone, encasing a small lobe of leprotic granuloma ( $\times 450$ ) in a juxta-articular node

Eliascheff,<sup>10</sup> Gougerot, Burnier and Eliascheff,<sup>11</sup> René Laclette<sup>12</sup> and A. Ullmo.<sup>13</sup> Another peculiarity is the flat discoid shape, the thick-

10 Jeanselme, E., Burnier, R., and Eliascheff, O. Considerations sur un cas de nodosité juxta-articulaire survenue chez un syphilitique, *Bull Soc franç de dermat et syph* **35** 450, 1928

11 Gougerot, H., Burnier, R., and Eliascheff, O. Un cas de nodos articulaire syphilitique, *Bull Soc franç de dermat et syph* **35** 907, 1928

12 Laclette, R. *Semiologia das dermatoses nodosas*, Thesis, Rio de Janeiro, 1938

13 Ullmo, A. Un cas de nodosite juxta-articulaire, *Bull Soc franç de dermat et syph* **41** 193, 1934

ness being less than half the width. No safe deduction can be drawn as to the value of this peculiarity, owing to the insufficiency of data available. Only total removal reveals the exact shape of the node, the usual clinical palpation is insufficient. In the present case palpation gave the false impression of a globular nodule. In Hudson's case,<sup>14</sup> the only one in which valuable data are mentioned, the syphilitic nodule was thicker, measuring 8 by 4 by 4 cm. These geometric data do not seem sufficient to give individuality to the leprotic node, but the association with active lesions of nodular leprosy (lepromatous) is the special feature in the case. A similar association is observed in many cases of syphilis in which the nodes appear simultaneously with tertiary manifestations.

The oldest report of juxta-articular nodes in leprosy appears in an original paper by Adolf Lutz<sup>1</sup> in which he regarded them merely as a casual occurrence, for he stated that nearly all patients were more or less suspected of having syphilis and that the lesions were cured by the use of potassium iodide. The other reference was made by Fred Wise,<sup>9</sup> but this was much more positive. In his case, although all the signs were favorable, no tests were made to demonstrate a new fact. The patient suffered from neural leprosy with maculoanesthetic lesions and neuritis of the ulna and nodules on the elbows, but no histopathologic proofs were offered, nor was *M. leprae* found in the lesions. Regression after treatment with chaulmoogia oil is not convincing proof, as, unfortunately, this drug is not specific for leprosy and its therapeutic action extends to other diseases, as was demonstrated by Lomholt<sup>15</sup> in cases of mycosis fungoides and Boeck's sarcoid.

#### SUMMARY

We have described a case of juxta-articular node in a patient with nodular leprosy (lepromatous). In the lesion there were found Virchow cells and numerous acid-resistant bacilli (within the node). Juxta-articular nodes of Lutz and Jeanselme should be regarded as a syndrome in which syphilis, yaws, tuberculosis or leprosy can be the causative factor.

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14 Hudson, E. H. Juxta-Articular Nodules in Euphrates Arabs, *Tr. Roy Soc. Trop. Med. & Hyg.* **28** 511, 1935.

15 Lomholt, S. Douze cas de sarcoïdes de Boeck traites à l'antileprol, *Bull. Soc. franç. de dermat. et syph. (Reunion dermat., Strasbourg)* **41** 1354, 1934.



# ACUTE IDIOPATHIC CIRCUMSCRIBED CUTANEOUS GANGRENE

Report of Two Cases

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MEDICAL CORPS, ARMY OF THE UNITED STATES

**G**ANGRENE is usually associated with circulatory deficiencies and infectious processes or a combination of both. However, a group of cases has been observed by dermatologists in which all available studies have revealed no organic or infectious cause for the sudden death of circumscribed areas of skin.

Trimble<sup>1</sup> presented a case of a circumscribed patch of gangrene of the thumb which was similar to these cases. Spillman<sup>2</sup> described the same phenomena in acute gangrene of the labium majus. Stopf<sup>3</sup> cited cases of spontaneous gangrene of the extremities in young adults in which causation was not revealed by thorough studies, and he ascribed the condition to constitutional weakness of the circulatory system. Touraine,<sup>4</sup> in the discussion of similar cases of acute idiopathic gangrene of the skin, postulated local infection, but unfortunately bacterial studies were not made.

Vohwinkel<sup>5</sup> described a patient with trophoneurotic gangrene of the skin. Twenty-one years previously, a bullet lodged in the right middle cranial fossa, after a shift of position, the bullet caused an irritation of the right trigeminal nerve. Areas of gangrene appeared in the skin innervated by the right trigeminal nerve, and after the bullet was removed there was prompt healing.

## REPORT OF CASES

CASE 1—H. W., a 23 year old white man, was admitted to the hospital on May 3, 1944, with a history of "white blisters" appearing on the dorsum of the left

From the Dermatology Section, Medical Service, Regional Hospital, Camp Joseph T. Robinson, Ark.

1 Trimble. Case of Spontaneous Gangrene, *Arch. Dermat. & Syph.* **3**: 454 (April) 1921.

2 Spillman, L. Spontaneous Gangrene of the Genitalia and Antigungrene Serum, *Bull. Soc. franç. de dermat. et syph.* **31**: 15, 1924.

3 Stopf, A. Spontaneous Gangrene of Extremities in Young Adults, *Arch. f. klin. Chir.* **158**: 297, 1930.

4 Touraine, A., Lortat-Jacob, E., and Neret. Benign Microbic Insular Gangrene of Skin, *Bull. Soc. franç. de dermat. et syph.* **45**: 1022, 1938.

5 Vohwinkel, K. H. Trophoneurotic Gangrene of Skin, *Arch. f. Dermat. u. Syph.* **152**: 75, 1926.

foot which rapidly became small black areas, enlarging and coalescing to form the large plaque and satellite lesion as illustrated by figure 1

There were no general symptoms. All laboratory examinations, including careful hematologic studies and studies of blood chemistry and urine, revealed only normal conditions. An edge of a gangrenous plaque was loosened, and materials for cultures were taken from what was considered the active spreading edge. Both aerobic and anaerobic cultures showed no growth. The result of the serologic test for syphilis was negative.



Fig 1 (case 1) —Acute idiopathic gangrene of seven days' duration (photograph by United States Army Signal Corps)

General physical examination revealed no evidence of a chronic systemic disease. The left anterior and posterior tibial arteries had strong pulsations. Neurologic examination revealed nothing abnormal. However, it was noticed that the patient had a tense and anxious mental attitude.

The possibility of self-inflicted lesions caused by some escharotic was briefly considered but quickly dismissed because of the size and shape of individual lesions and because of repeated observations in the three day period necessary for the development of the disease as illustrated (fig 1).

After the third day the mummified areas of skin did not enlarge. The slight inflammatory areola faded gradually, and after two weeks the ingrowth of epithelium lifted up the edges of the plaques. In approximately seven weeks, the areas were replaced by a smooth pliable scar.

Treatment consisted only of daily dusting with sulfathiazole powder and application of dry heat. No dressings were used.

CASE 2—C S, a man aged 22, was admitted to the hospital on Jan 4, 1945, with the history that his left foot had been feeling numb for about a week. Then,



Fig 2 (case 2)—Circumscribed acute gangrene of two weeks' duration (photograph by United States Army Signal Corps)

according to the patient's description, "white blisters" appeared, which became the multiple black dry areas illustrated (fig 2). Gangrenous plaques ceased to develop after three days. The temperature remained normal through the acute stage.

All laboratory studies, including aerobic and anaerobic cultures of material obtained by loosening an edge of mummified skin, failed to reveal any abnormalities. General physical and neurologic examinations showed no evidence of

disease Self-produced lesions were ruled out by the size and shape of the lesions and close observation Good local arterial pulsations were present

Treatment was the same as in the previous case Healing took approximately seven weeks

#### COMMENT

Acute idiopathic circumscribed gangrene of skin is characterized by (1) spontaneous onset in apparently healthy persons, (2) approximately a three day "active period" in which a small vesicle initially appears, the involved area quickly becomes black and enlarges to a gangrenous plaque, and during the active stage a cyanotic areola is present, (3) negative results of physical, neurologic and laboratory studies, (4) healing in about six to eight weeks, with a smooth scar remaining in involved areas

I can only speculate as to the cause of this peculiar type of cutaneous gangrene It may be a trophoneurotic phenomenon, since it is well known that varied lesions of the skin can be produced under hypnosis A similar mechanism may be present in these cases

## ISOLATION OF DERMATOPHYTES

A New Procedure for Use in the Presence of Saprophytic Fungi, Especially in Mixed Cultures and from Leather

J M LEISE, M S

AND

L H JAMES, Ph D

COLLEGE PARK, MD

VARIOUS investigations in this laboratory have required the microbiologic examination of worn shoes, with the microflora present being large in number and varied in type and including many molds. Generally, the saprophytic molds far outnumber and outgrow the pathogenic types, so that isolation or determination of the numbers of pathogens is nearly impossible. Therefore a medium capable of a selective preference for the dermatophytes over the saprophytes would be beneficial.

The mediums commonly used for the cultivation of pathogenic fungi have no inherent differential powers for the isolation of dermatophytes when saprophytes are present. Various investigators have reported difficulty in the isolation of dermatophytes from highly contaminated sources. Weidman<sup>1</sup> wrote that "several workers (personal communications) have failed in attempts to demonstrate dermatophytes in old shoes, etc., in each case it was on account of the rank overgrowth of saprophytic molds. Even were the dermatophytes present and growing, they could not have been recognized."

Bonar and Dreyer<sup>2</sup> were not able to cultivate dermatophytes from hair found in dressing rooms and shower rooms and showing the presence of pathogenic fungi under microscopic examination because of "the great difficulty of isolating these comparatively slow growing organisms from such material."

Neal and Emmons<sup>3</sup> stated that "failure to isolate any dermatophytes from the floors of showers and locker rooms was probably due to the

From the Department of Bacteriology, University of Maryland

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Maryland

1 Weidman, F W Ringworm Fungi, Pennsylvania M J **34** 695-701 (July) 1931

2 Bonar, L, and Dreyer, A D Studies on Ringworm Funguses with Reference to Public Health Problems, Am J Pub Health **22** 909-926 (Sept) 1932

rapid growth of more vigorous organisms and the consequent suppression of pathogens. Probably an improvement in the technic of examination and isolation would have revealed the presence of ringworm fungi on the floors."<sup>4</sup>

## HISTORICAL SURVEY

The effects of  $p_H$  on the growth of dermatophytes and saprophytic fungi have been studied by many investigators. In 1926, Keller<sup>5</sup> found that the "Kaufman-Wolf fungus" developed in mediums of a wide  $p_H$  range, from 6.8 to 12.0 with the optimum being from  $p_H$  6.8 to 7.0. He also found that *Epidermophyton inguinale* developed in a  $p_H$  range of 6 to 10 and grew best in a medium of  $p_H$  7.0.

Tate<sup>6</sup> referred to Verujsky (1887) as having found a neutral or slightly acid medium most favorable for growth of *Trichophyton tonsurans* and *Achorion schoenleinii*, with the optimum temperature being about 33°C. Tate, using both Sabouraud's and synthetic mediums, found wide  $p_H$  ranges for growth of the dermatophytes. The limit for growth on the acid side was 3.0 to 4.0, while it was "beyond  $p_H$  8.0" on the alkaline side, the optimum  $p_H$  being about 6.0 to 7.0. He stated that all the dermatophytes were found to have an active proteolytic enzyme which acts in an alkaline medium and can hydrolyze intact proteins (casein) with the production of free amino acids. This enzyme resembles trypsin, no pepsin being found. The proteolytic enzyme of *Aspergillus niger* acts in a strongly acid medium and resembles pepsin.

In 1929, Kadisch<sup>7</sup> found that the best growth of the dermatophytes on Sabouraud's maltose agar, 3 per cent peptone agar and Gutz glycerin agar occurred at  $p_H$  7.2 to 7.6. He found a tendency for cultures started on the acid side to become alkaline as a result of fungal activity. He also<sup>8</sup> found 37°C unfavorable for *Achorion gypseum*.

3 Neal, P. A., and Emmons, C. W. Dermatitis and Coexisting Fungous Infections Among Plate Printers, Bulletin 246, United States Treasury Department, Public Health Service, April 1939.

4 Peck, Botvinick and Schwartz recently reported (Peck, S., Botvinick, I., and Schwartz, L. Dermatophytosis in Industry, Arch Dermat & Syph **50** 170-178 [Sept.] 1944) that they did not recover dermatophytes from samplings of pine lattice floorings and concrete shower floors.

5 Keller, P. Zur Klinik der Hyphomykosen, insbesondere der dyshydrosiformen Epidermophytien. Zugleich ein Beitrag zur regionalen Verbreitung der Hyphomyzeten, die Pilzflora Oberbadens, Dermat Ztschr **49** 33-51 (Oct.) 1926.

6 Tate, P. Dermatophytes or Ringworm Fungi, Biol Rev **4** 41-75 (Jan) 1929.

7 Kadisch, E. Ueber die Bedeutung der Nährbodenalkalität in der Mykologie, Dermat Ztschr **55** 385-396 (April) 1929.

8 Kadisch, E. Beiträge zur Lehre von den Dermatomykosen. III. Ueber das Wachstum von *Achorion gypseum* auf Meerschweinchenorganen und über die Zuchtungs-temperatur, Arch f Dermat u Syph **158** 480-484, 1929.

Biltris<sup>9</sup> grew *Trichophyton gypsum* (asteroides) on peptone 3 per cent and agar 1.8 per cent, with the medium at initial  $p_H$  values of 3.8, 6.0 and 11. No fuseaux occurred at  $p_H$  11.

Von Mallinckrodt-Haupt<sup>10</sup> found that *T. gypsum* grown in buffered solutions for several months made an acid medium basic and a basic solution almost neutral. This was true also for *Achorion quinckeanum*, but it made the basic medium more acid ( $p_H$  6.10 to 6.92 from  $p_H$  8.0). When these fungi were started on mediums at  $p_H$  6.01 to 7.19, they changed the  $p_H$  to the basic side of neutrality, while *Penicillium glaucum* and "*Rosa Lufthebe*" made the same mediums more acid. These differences are explained by the ability of the pathogens to break down the protein source of nitrogen.

In 1930, Talice<sup>11</sup> presented data which showed *Sabouraudites granulosis* (on Sabouraud's proof medium) able to grow at a minimum of  $p_H$  4 and a maximum above 9.6. Both *Penicillium citrinum* and *Rhizopus nigricans* were able to grow at  $p_H$  2.2, with their minimum  $p_H$  being below this. Their maximum  $p_H$  was, as was that of *S. granulosis*, above 9.6. The optimum of *S. granulosis* was given as  $p_H$  6 to 7.

Levin and Silvers<sup>12</sup> found the reaction of the fourth interdigital space of the foot to vary in different persons from  $p_H$  6.30 to 7.85. The higher value was obtained in a case of severe dermatophytosis. Another high value,  $p_H$  7.65, was obtained and this too was in a case of active dermatophytosis of the foot.

Von Mallinckrodt-Haupt,<sup>13</sup> in discussing the change in reaction which the molds produce in the growth medium, stated that true dermatophytes, with the exception of the *Epidermophyton* fungi, showed strong tendencies toward the formation of alkali while most of the saprophytic hyphomycetes produced acid.

Cerutti<sup>14</sup> stated that *T. gypsum* always gives an alkaline reaction during its development, while the "*Achorion of Schoenlein*" and the

9 Biltris, R. Sur la variabilité des caractères de l'espèce chez les dermatophytes, *Ann Inst Pasteur* **43** 281-358 (March) 1929.

10 Von Mallinckrodt-Haupt, A.  $p_H$  Messungen bei Pilzkulturen, *Dermat Ztschr* **55** 374-384 (April) 1929.

11 Talice, R. V. Le facteur  $p_H$  en mycologie, son influence sur la culture de certaines espèces de champignons parasites de l'homme, *Ann de parasitol* **8** 183-188 (March) 1930.

12 Levin, O. L. and Silvers, S. H. The Possible Explanation for the Localization of Ringworm Infection Between the Toes, *Arch Dermat & Syph* **26** 466-470 (Sept) 1932.

13 Von Mallinckrodt-Haupt, A. Der Wert der  $p_H$  Messung bei Pilzkulturen, *Zentralbl f Bakt (Abt 1)* **125** 368-374 (Aug 27) 1932.

14 Cerutti, P. Concentrazione idrogenionica e sviluppo degli ifomiceti patogeni. Ricerche sperimentali e cliniche, *Pathologica* **25** 32-37 (Jan 15) 1933.

"Sporotrichum of Gougeiot and Schenck" gave an acid reaction at the beginning that later turned toward alkalinity

Belisario<sup>15</sup> stated that "the predilection of mycological infections for the palms and soles is due to the alkaline tendency of the sweat in these areas" Where sebaceous glands are richly supplied, mycotic infections are rarely found, he stated, and "the hyperactivity of the sebaceous glands at puberty, through increasing the hydrogen-ion concentration of the scalp sweat, may afford a feasible explanation of the disappearance of certain small-spore ringworms at that age"

Williams<sup>16</sup> noted an apparent slight increase in growth of *T. gypsum* when the  $p_H$  of the medium (cysteine) was raised from 5.4 to 6.6

Peck and Rosenfeld,<sup>17</sup> using "Sabouraud's bouillon" unbuffered, obtained growth of *T. gypsum* in the range of  $p_H$  3.4 to 10.0 inclusive. No growth occurred at  $p_H$  3.0. Using McIlvaine's buffers, they obtained growth from  $p_H$  3.4 to 9.0. Plates poured with buffered mediums showed growth throughout the whole  $p_H$  range (4 to 10) studied, but *T. gypsum* showed definite retardation at all  $p_H$  values except 7.0 and 8.0. *E. inguinale* was retarded through the series. *T. gypsum* was found to increase the  $p_H$  once growth started, and at the end of three weeks without buffer it raised the  $p_H$  from 5.0 to 7.6, whereas with buffer the  $p_H$  rose to 6.5. As all the nonbuffered solutions rose to a  $p_H$  of 7.6 to 8.0, Peck and Rosenfeld concluded that the "optimum"  $p_H$  range for *T. gypsum* must lie here. They expressed the belief that the presence of a buffer when it interferes with the production of a  $p_H$  value optimum for growth retards the growth of the organism and that this fact explains the less vigorous growth obtained with buffered solutions as compared with that obtained in nonbuffered solutions.

Peck and Rosenfeld noted that in unbuffered mediums up to  $p_H$  8.0 the growth of *T. Gypsum* resulted in a significant rise in the  $p_H$ , at 8.0 there was only a slight increase in  $p_H$ , and at  $p_H$  9.0 and 10.0 a change to a more acid reaction took place, the  $p_H$  dropping to 8.08 and 7.87 respectively. With buffers the  $p_H$  increased less and dropped more (except at  $p_H$  3.4), there being a sharp drop from  $p_H$  8.0, 9.0 and 10.0.

We<sup>18</sup> made a study of the relationship between  $p_H$  tolerance and the pathogenicity of fungi, and it was found that the dermatophytes were

15 Belisario, J. C. Mycotic Infections and Their Treatment, *Brit. M. J.* **1** 404-406 (Feb. 29) 1936.

16 Williams, J. W. Subsurface Growth of Pathogenic Fungi on Peptone, Hair, Pig Skin and Cysteine-Cystine Mediums, *Arch. Dermat. & Syph.* **36** 581-598 (Sept.) 1937.

17 Peck, S. M., and Rosenfeld, H. The Effects of Hydrogen Ion Concentration, Fatty Acids and Vitamin C on the Growth of Fungi, *J. Invest. Dermat.* **1** 237-265 (Aug.) 1938, correction, *ibid.* **1** [398a] (Oct.) 1938.



capable of growing on an alkaline medium (Sabouraud's dextrose agar adjusted to an initial  $p_H$  of 10.5) whereas saprophytic fungi were largely inhibited. The alkaline medium was used for the isolation of dermatophytes in the presence of rapidly growing saprophytes.

#### EXPERIMENTAL STUDY

*General Methods* The purpose of this research was to devise a medium capable of selecting or favoring dermatophytes over saprophytic fungi. The growth of these two types of fungi was studied in separate and in mixed cultures.

*Organisms* The saprophytic fungi used in this investigation consisted of *Aspergillus niger*, *Rhizopus nigricans* and *Penicillium* species 8 and 34, the latter species having been isolated from worn shoes. These three genera are the ones commonly occurring on shoes and floors. The dermatophytes<sup>19</sup> used were *Epidermophyton floccosum* no. 0 and no. 23, *Trichophyton interdigitale*, *Trichophyton purpureum*, *Trichophyton mentagrophytes*, *Trichophyton rubrum*, *Trichophyton sulfureum*, *Trichophyton gypseum* no. 2 and no. 20 and *Microsporum lanosum*. Suspensions of the cultures were made with water, and pour plates were made, using the suspension as the inoculum.

*Media and Incubation* Sabouraud's dextrose or maltose agar of the following composition was used in the experiments reported here: peptone (Bacto), 10 Gm, dextrose or maltose (Bacto), 40 Gm, agar (Bacto), 15 Gm, and water, 1,000 cc. No adjustment of the  $p_H$  was made prior to sterilization at 15 pounds (6.8 Kg) of steam pressure for twenty minutes.

Immediately before plates were poured, the  $p_H$  of this medium was adjusted by the addition of normal sterile sodium hydroxide solution to the bottles of melted agar. Adjustment to  $p_H$  10.5 was made by the use of La Motte purple. This was later checked with a Beckman  $p_H$  meter. The mediums were not buffered, and it is recognized that the  $p_H$  was lowered during incubation. Thus the  $p_H$  values given are the initial values only, and the term "alkaline medium" refers to Sabouraud's dextrose or maltose agar adjusted to an initial  $p_H$  of 10.5. The time of incubation at 34°C is indicated in the text and the tables.

*Isolation from Mixed Cultures* A comparison of the alkaline medium was made with Sabouraud's dextrose agar<sup>20</sup> of unadjusted

18 Leise, J. M., and James, L. H. An Alkaline Medium and Procedure for the Selection of Dermatophytes in the Presence of Saprophytic Fungi, *J. Lab. & Clin. Med.* **30** 119-131 (Feb.) 1945.

19 *Trichophyton mentagrophytes* and *Trichophyton sulfureum* were supplied by Dr. C. W. Emmons, of the National Institute of Health, Bethesda, Md., and *T. rubrum*, *T. gypseum* no. 2, *E. floccosum* no. 23 and *M. lanosum* were supplied by Dr. E. M. Rockwood, Massachusetts General Hospital, Boston.

20 Sabouraud's maltose agar was used in the previous study,<sup>18</sup> but, since Sabouraud's dextrose agar is more commonly used in the cultivation of dermatophytes, dextrose was used thereafter except in the study reported in table 3. Experience showed that Sabouraud's dextrose agar at an initial  $p_H$  of 10.5 with incubation at 34°C gave results as good as and sometimes better than the maltose agar in Sabouraud's formula.

$p_H$  (5.5), using all ten pathogenic dermatophytes individually combined with *R. nigricans*, *A. niger* and *Penicillium* species 8. One drop of a suspension of each of the cultures was used in this preliminary experiment to obtain an estimate of the extent of inhibition produced by the alkaline medium. The selective action of the alkaline medium at 34 C

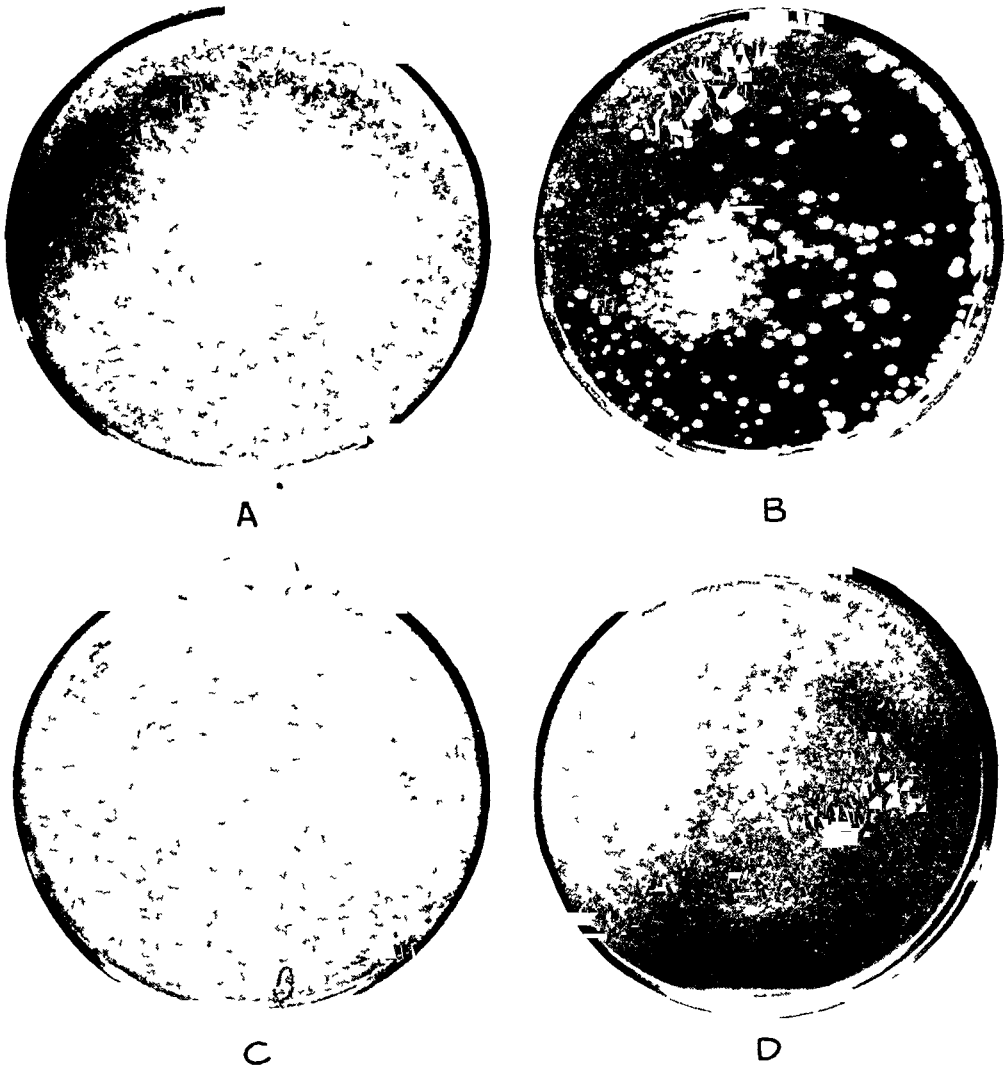


Fig 1—The selective action of the alkaline medium for *T. mentagrophytes* in the presence of *R. nigricans*. (Plates *A* and *C*, Sabouraud's dextrose agar  $p_H$  5.5, plates *B* and *D*, alkaline medium, plates incubated for five and a half days at 34 C). Plates *A* and *B* contain the same approximate inoculum of 10,000 *R. nigricans* mixed with 400,000 *T. mentagrophytes*. Plates *C* and *D* contain the same approximate inoculum of 1,000 *R. nigricans* in pure culture.

was shown rather strikingly when *R. nigricans* was the saprophytic fungus combined with the dermatophytes. Here, all ten dermatophytes were each prevented from showing growth on Sabouraud's dextrose

again ( $p_H$  5.5) because of the rapid and heavy overgrowth by *R. nigricans* (fig 1, plates *A* and *C*) However, on the alkaline medium this saprophyte was completely inhibited in all instances after five and a half days of incubation at 34 C (fig 1, plates *B* and *D*) The use of *A. niger* as the saprophytic test fungus gave similar results This saprophyte

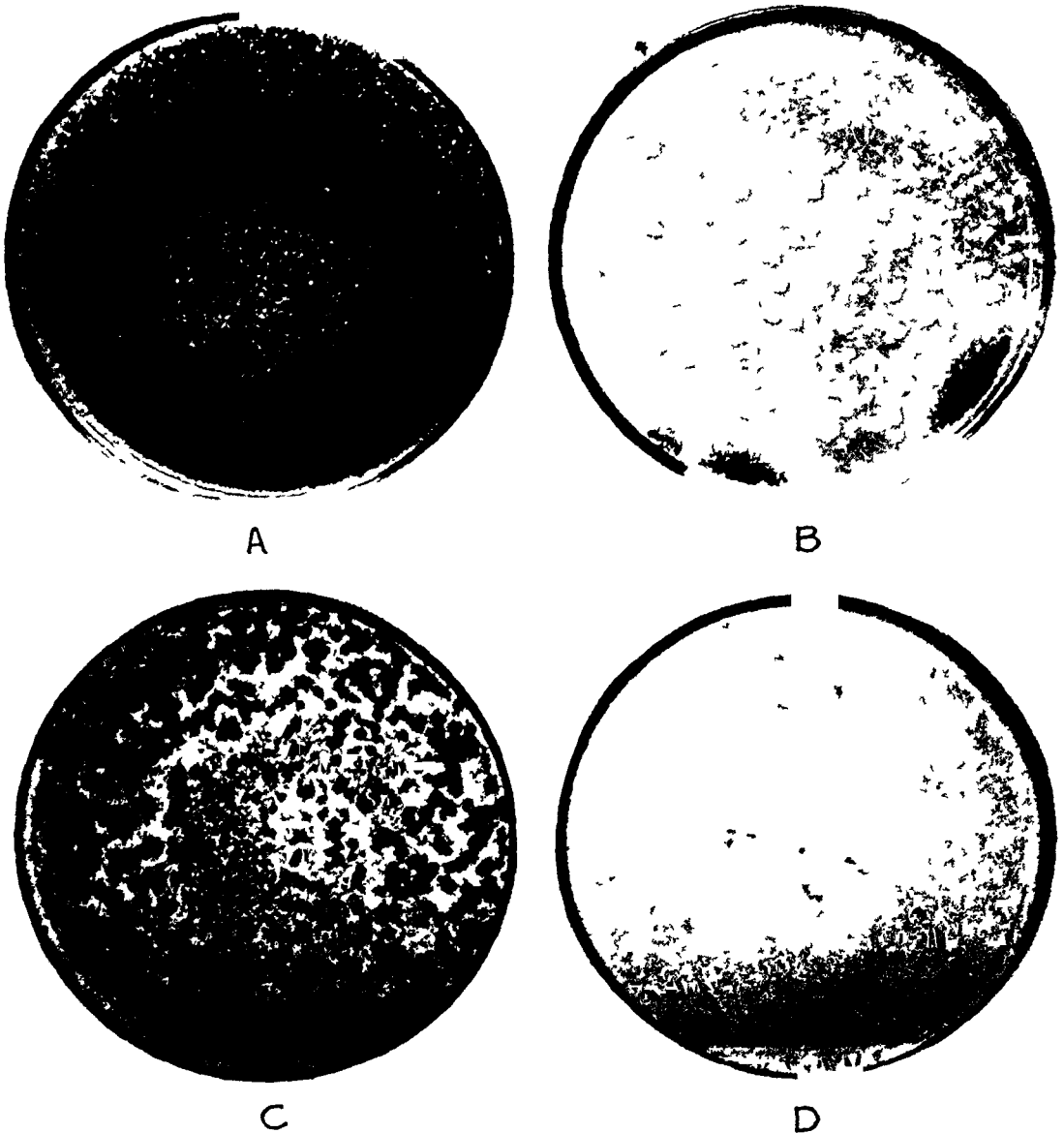


Fig 2—The selective action of the alkaline medium for *T. mentagrophytes* in the presence of *A. niger* (Plates *A* and *C*, Sabouraud's dextrose agar  $p_H$  5.5, plates *B* and *D* alkaline medium, plates incubated for five and a half days at 34 C) Plates *A* and *B* contain the same approximate inoculum of 5,500 *A. niger* mixed with 40,000 *T. mentagrophytes* Plates *C* and *D* contain the same approximate inoculum of 55,000 *A. niger* in pure culture

grew so rapidly and vigorously on the unadjusted medium that no growth of the dermatophytes was obtained (fig 2, plates *A* and *C*) The alkaline medium, however, showed heavy growth with each of the

ten dermatophytes and, in addition, inhibited *A. niger* (see fig 2, plates *B* and *D*) Only a slight growth of *E. floccosum* no 23 occurred while *A. niger* showed fair growth when these two fungi were combined *E. floccosum* no 23 grows very slowly, and the growth of *A. niger* on the plate where the dermatophyte showed little growth is typical of other observations That is, the alkaline medium inhibits the growth of the saprophytic fungi while the dermatophytes grow At times these saprophytes overcome the primary inhibition of the alkaline medium and show slight to good growth The results of this study show that the alkaline medium is highly effective in selecting dermatophytes over *A. niger*

The inhibition of *Penicillium* by the alkaline medium is considerably less than that of *Rhizopus* and *Aspergillus* Although more study is required, it appears that *Penicillium* varies more than the other two saprophytic genera in their susceptibility toward inhibition by the alkaline medium Also, subsurface colonies of *Penicillium* on the alkaline

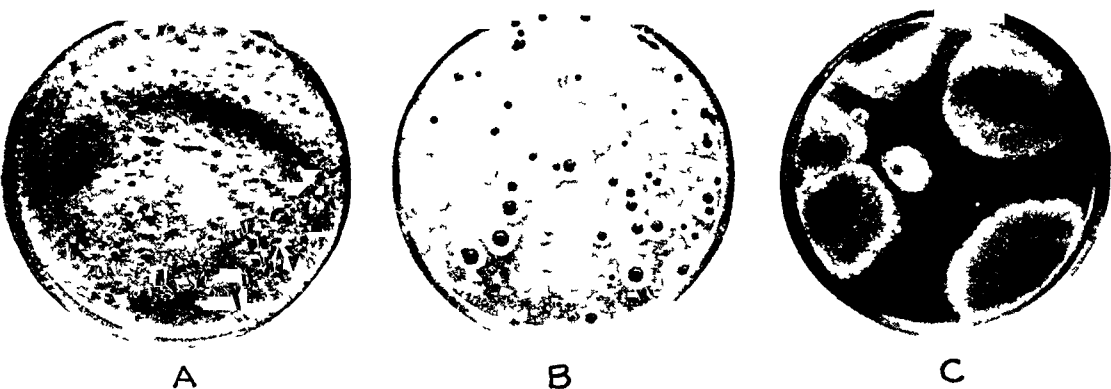


Fig 3—The selective action of the alkaline medium for *T. mentagrophytes* in the presence of *Penicillium* species 34 (Plates *A* and *C*, Sabouraud's dextrose agar  $pH$  5.5, plate *B*, alkaline medium, plates incubated for five and a half days at 34 C) Plates *A* and *B* contain the same approximate inoculum of 104,000 *Penicillium* species 34 mixed with 400,000 *T. mentagrophytes* Plate *C* shows the spreading colonies of *Penicillium* on Sabouraud's dextrose agar in a higher dilution

medium may be confused with the dermatophytes However, the *Penicillium* colonies are fewer in number, smaller in size and do not spread (fig 3, plate *B*) Table 1 shows the effectiveness of the alkaline medium in selecting *T. mentagrophytes* from a mixed inoculum containing this dermatophyte and *Penicillium* sp 34

Although the alkaline medium had been shown to be superior to Sabouraud's dextrose agar in isolating dermatophytes from mixed cultures, it was still a question whether it would be effective when the saprophytic contamination was great and the numbers of pathogens were small Therefore, suspensions were prepared of *A. niger* and *E. floccosum* 23 and known numbers of each were combined This mixed

suspension was then inoculated into Petri dishes and poured with Sabouraud's dextrose agar and the alkaline medium. When 166 *E. floccosum* 23 (counted on the alkaline medium) were combined with 125,000 *A. niger* (counted on the Sabouraud dextrose agar, using serial dilutions) and were poured with Sabouraud's dextrose agar, the plates were black with *A. niger* growth in two and a half days, and any potential colonies of pathogens would not have been able to appear. Such plates held for seven days showed no growth of pathogenic types. However, when the alkaline medium was used, 40 *E. floccosum* 23 colonies appeared, while about one half of the plate was covered with aspergillus growth. The *E. floccosum* 23 inoculum was reduced from

TABLE 1—*The Selective Action of Sabouraud's Dextrose Agar and the Alkaline Medium on a Mixture of T. Mentagrophytes and Penicillium Species 34*  
Pour plates incubated ten days \*

Culture	Dilution of Plates	Sabouraud's Dextrose Agar	
		pH 5.5	pH 10.5
<i>T. mentagrophytes</i>	1:1	Plate all white	Plate all white
	1:10	Plate all white	Plate all white
	1:100	Plate all white	210 colonies
<i>Penicillium</i> sp. 34	1:1	Plate all green	Plate all green
	1:10	Plate all green	101 colonies
	1:100	Plate all green	12 surface colonies 50 small subsurface colonies
<i>T. mentagrophytes</i> and <i>Penicillium</i> sp. 34	1:1	Plate all green	Plate all green
	1:10	Plate all green	82 <i>Penicillia</i> 84 <i>T. mentagrophytes</i>
	1:100	Plate all green	49 <i>Penicillia</i> 38 <i>T. mentagrophytes</i>

\* Seven days at 34° C. followed by three days in the room.

166 to 26, but failed to show growth on either medium when combined with the *A. niger* as above. It should be noted that the saprophytic inoculum per Petri dish was high (125,000) and that *E. floccosum* 23 is the slowest growing of all the dermatophytes tested.

Part A of table 2 gives the results obtained when 124,000 *A. niger* were combined with 3,440 and 344 *T. purpureum* and plated with the alkaline medium. Where the ratio<sup>21</sup> was 1 *T. purpureum* to 36 *A. niger* the entire alkaline plate was covered with *T. purpureum* growth, with *A. niger* appearing only as a spot at the edge of the plate. No pathogenic growth occurred on the alkaline medium when the ratio was 1 *T. purpureum* to 360 *A. niger*, only *Aspergillus* grew.

<sup>21</sup> All the ratios presented in this paper are given as indications of the effectiveness of the alkaline medium compared to Sabouraud's dextrose agar (pH 5.5). They are not to be taken as definite mathematical data.

aud's agar, with no dermatophytes present, whereas growth of the dermatophyte was obtained on the alkaline medium. The only saprophytic fungus present was *Penicillium*, but the colonies were small and did not show spreading growth. These results were obtained after five days' incubation, while after eleven days' incubation *T. gypsum* 2 was overgrowing the green *Penicillium* colonies.

#### COMMENT

The alkaline medium has been successfully used in this laboratory for the reisolation of dermatophytes that had been inoculated on leather and treated with fungicides. In these studies the leather frequently was from worn shoes and carried a varied and heavy contamination of bacteria and saprophytic fungi. Experience in these tests corroborated the previous experimental findings in that most of the saprophytic fungi were inhibited so as not to interfere with the pathogens. Of the saprophytes that grew, *Penicillium* most often appeared on the plates, the colonies of which were small and nonspreading. This allowed growth of the dermatophytes to appear, which growth may be due to the presence of more space in the medium and/or to less antagonism produced by other fungal growth. It has been observed that whereas the *Penicillium* overgrows the surface of Sabouraud's dextrose agar it is the dermatophyte that usually overgrows the *Penicillium* colonies on the alkaline medium.

*Rhizopus* practically never appears, while *Aspergillus* may appear as small surface colonies. The spore formation of such saprophytes as *Aspergillus* and *Penicillium* is also inhibited. *Aspergillus* first appears as yellow and *Penicillium* as white colonies. Growth is also slower on the alkaline medium than on unadjusted Sabouraud's dextrose agar and plates may appear sterile for three days before growth begins to appear, for  $p_H$  10.5 is by no means the optimum  $p_H$  for the growth of the dermatophyte but was derived from the study of  $p_H$  tolerance. After three days' incubation, growth proceeds more rapidly. General observations indicate that more colonies of the dermatophytes may be fluffy on the alkaline medium than on Sabouraud's agar, but granular colonies will also appear. If the fluffy colonies are transferred to ordinary mediums as soon as growth appears, granular colonies often develop.

*Penicillium* may appear as small white subsurface colonies when inoculated plates have been poured with the alkaline medium and might be mistaken for colonies of dermatophytes. Nevertheless, the "pour plate" method is to be preferred over the "streaked plate" method, for the saprophytic fungi produce a more rapid and profuse growth when streaked on the surface of the alkaline medium than when plates are poured, and a much better selection of dermatophytes is obtained by use of the pour plate method.

Experience has shown that the alkaline medium gives best results when incubated at 34 C for five and a half to six days. After this time plates are counted, and suspicious colonies picked to ordinary Sabouraud's dextrose agar, or the plates are incubated for longer periods except when they already show overgrowth with colonies of saprophytic fungi. Saprophytic fungi may overgrow any dermatophytes present when incubation extends beyond six days, hence the plates must be examined after five and a half to six days. A temperature of 37 C is not recommended because of a slightly greater inhibiting effect on the dermatophytes. Fluctuating "room" temperatures also are not recommended, for *Aspergillus* and possibly other saprophytes are favored. Hydrogen ion concentrations higher than  $p_H$  10.5 are not more effective in inhibiting *Penicillium*. The alkaline medium is not buffered, and the  $p_H$  of the sterile agar in a Petri dish incubated at 34 C drops to about  $p_H$  9.4 within one day and remains at approximately  $p_H$  9.0 thereafter through the fourteenth day. Further studies on the importance of this factor are in progress.

The alkaline medium has also been used for the isolation of dermatophytes from normal worn shoes. Numerous examinations of worn shoes in this laboratory and elsewhere have shown the presence of saprophytic molds in large numbers, particularly on the insole. Heretofore there has been no technic by which the numbers of dermatophytes in shoes could be determined, and no such data have yet been compiled to our knowledge. Undoubtedly the numbers will vary widely under different conditions of infection, perspiration, foot sanitation and other factors. It is likely that in many instances the numbers of dermatophytes will be small in relation to the numbers of saprophytic fungi, so that in order to detect the dermatophytes platings must be made in low dilutions. Therefore, it is especially interesting to record the results of a study using the alkaline medium for the examination of worn shoes. Reed<sup>23</sup> has isolated seventeen pathogenic fungi of *Trichophyton*, *Epidermophyton* and *Microsporum* genera from twenty-five pairs of shoes and twelve pairs of socks using our alkaline medium. In his work Sabouraud's dextrose agar was used along with the alkaline medium, and in no instance was a dermatophyte found on the unadjusted plates.

Cultures of dermatophytes contaminated with saprophytic molds have been regained in pure culture by use of the alkaline medium. A successful procedure has been to make a transfer of a piece of the contaminated dermatophyte colony into a small bottle containing sterile water and glass beads. This is shaken and then plated with the alkaline medium.

23 Reed, E. L. A Study of the Microflora of Shoes, Socks and Feet. Master of Science Thesis, University of Maryland Library, 1943, unpublished data.

Preliminary tests in the use of alkaline agar slants for the isolation of dermatophytes from cutaneous scales contaminated with saprophytic fungi have been successful. The freshly prepared alkaline slants (or solidified agar plates) may be implanted with scrapings of skin and incubated as we have described. Further studies along these lines and on the use of bacterial inhibitors are contemplated.<sup>24</sup>

The correlation between pathogenicity and  $p_H$  tolerance is striking in the data presented here. This relationship is not in disagreement with any of the various studies reviewed in the historical part of this paper, concerning the  $p_H$  tolerance of fungi: the differences in  $p_H$  tolerance between enzymes of dermatophytes and a saprophytic fungus (such as *A. niger*), the alkalinity of areas (such as the interdigital spaces of the foot) favoring growth of the dermatophytes or the subsequent clearing of infections of the scalp after puberty has increased the concentration of hydrogen ions in sweat from the scalp.

Tate's work<sup>6</sup> showing the presence of a trypsin-like enzyme in pathogenic fungi is significant, since this may explain why the dermatophytes are capable of growing comparatively well on the alkaline medium while the saprophytic fungi, such as *R. nigricans*, *A. niger* and *Penicillium*, generally do not. The relationship between pathogenicity and a tolerance of alkalinity is further supported by studies to be reported later with virulent and nonvirulent bacterial cultures of the same species.

#### SUMMARY AND CONCLUSIONS

The inhibition of saprophytic fungi by the alkaline medium while allowing the dermatophytes to grow is of interest.

1. A medium of high alkalinity (initial  $p_H$  10.5) has been presented for the isolation and counting of dermatophytes when in the presence of rapidly growing saprophytic fungi.

2. Evidence has been presented to show that the medium usually inhibits *R. nigricans* entirely, *A. niger* considerably and *Penicillium* Sp. to an appreciable extent while allowing the dermatophytes to grow. This enables isolation and detection of dermatophytes when it would be difficult or impossible to do so on ordinary Sabouraud's dextrose agar.

3. Preliminary results have shown the alkaline medium to be advantageous in the isolation of dermatophytes from cutaneous scales when

24. At times bacterial growth on the alkaline medium is profuse, and the use of 0.05 per cent copper sulfate, as suggested by Ch'in (Ch'in, T. L. Potassium Tellurite and Copper Sulfate in Sabouraud's Medium for Isolation of Pathogenic Fungi, *Proc. Soc. Exper. Biol. & Med.* **38** 700-702 [June] 1938), to inhibit bacteria in Sabouraud's dextrose agar may be of value in the alkaline medium.



saprophytic fungi are present as compared with Sabouraud's dextrose agar of unadjusted  $p_H$

4 Contaminated cultures of dermatophytes may be purified by use of the alkaline medium

5 The relationship of  $p_H$  pathogenicity has been emphasized

Mr E L Reed assisted in certain of the experiments

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## ELECTROSURGICAL REMOVAL OF PLANTAR WARTS (LOOP TREATMENT)

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A PRELIMINARY report on a method of treatment for plantar warts by electrosurgical removal was published in 1942<sup>1</sup>. It covered observations for only 21 patients. Since that time I have treated 106 additional patients with the same method, therefore, the conclusion drawn in the preliminary report can be considered now as well established.

The high frequency cutting current is used as a means to destroy the plantar wart, and the source of the current should be a long wave diathermy machine capable of producing a cutting current of the necessary quality and quantity. Short wave diathermy machines are not generally satisfactory for the purpose. There are two principal reasons for this:

1 Because of the extremely short wavelength, standing waves are produced on the electrode, as a result of which a machine which may have been properly calibrated on tissue specimens no longer holds its calibration when applied directly to the patient. This makes the adjustment, tuning and setting of the machine altogether too critical and too uncertain for a successful surgical technic.

2 The extremely high frequency of the short wave currents results in a tremendous reduction in the electrical impedance of the tissue at the point of contact of the cutting instrument. This causes a dispersion of the current from the cutting instrument in all directions, with a small heating action resulting in a shallow coagulation. In consequence, the coagulated sheath of tissue which walls off the nutrient channels of the growth in a proper electrosection is missing, and the required destruction of the growth is not accomplished.

The technic (which is simple) was described in the preliminary report.

As regards the indifferent electrode, it should be noted that in some cases it may be preferable to place it in direct contact with the body of the patient, depending on the make of the high frequency apparatus used.

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Dr. George Miller MacKee, Director.

1 Karp, F. L., and Frank, S. B. Electrosurgical Removal of Plantar Warts, *Arch. Dermat. & Syph.* **45**: 328-333 (Feb.) 1942.

In these cases, in order to avoid a possible spark and therefore a possible burn, this electrode should be covered with a layer of K-Y lubricating jelly or a lather of ordinary shaving cream. The electrode is then tightly applied to the lower part of the corresponding leg.

In concluding this report, I wish to say that out of the total of 127 patients (some with multiple lesions) treated with the loop method only 7 have not responded favorably to the treatment. In this series of 127 patients many had received previous treatments, including roentgen irradiation, without benefit.

The percentage of cures in the 127 patients is 95.51 per cent. All warts were of the common plantar type. No mosaic plantar warts were treated.

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## TYROTHRICIN IN THE TREATMENT OF DISEASES OF THE SKIN

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AND

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AND

JACK JONES, M D

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WITH the isolation of agents which are antagonistic to pathogenic micro-organisms, extensive investigation has been carried out in order to best utilize these antibiotics. Startling and almost miraculous results have been obtained by penicillin, which was isolated by Fleming<sup>1</sup> in 1929. R. J. Dubos<sup>2</sup> in 1939 first reported on the germicidal agent tyrothricin extracted from cultures of a soil bacterium. It is our purpose to review the results obtained in the treatment of some cutaneous diseases with the use of wet dressings and ointment containing tyrothricin.

The tyrothricin obtained was the concentrate which when properly diluted yielded an isotonic solution which contained 0.5 mg of tyrothricin per cubic centimeter. This was obtained in 20 cc vials and was diluted to 1,000 cc with sterile distilled water. This was applied to the affected areas as a wet dressing, so that the lesions were constantly dampened with the tyrothricin solution. To prevent the solution from evaporating rapidly the saturated gauze was well covered with oil cloth. For the ointment applications, each gram of greaseless base containing 0.3 mg tyrothricin in true solution was used.

Forty-seven patients with the following cutaneous infections were used as subjects for therapeutic trial.

Disease	No of Cases
Sycosis vulgaris	7
Acne (pustular)	5
Impetigo contagiosa	8
Dermatitis seborrheica with secondary infection	4
Ecthyma	2
Fungus (trichophyton) secondarily infected	6

1 Fleming, A. On Antibacterial Action of Cultures of *Penicillium* with Special Reference to Their Use in Isolation of *B. Influenzae*, *Brit J Exper Path* 10 226 (June) 1929.

2 Dubos, R. J. Bactericidal Effect of Extract of Soil *Bacillus* on Gram Positive Cocci, *Proc Soc Exper Biol & Med* 40 311 (Feb) 1939.

Disease	No of Cases
Decubitus ulcer	5
Pyoderma (children)	3
Dermatitis repens	2
Acrodermatitis perstans	3
Nummular eczema	2
Total	47

Our intention was to determine the effectiveness of tyrothricin in the treatment of disease caused by pyogenic organisms or in diseases in which there was secondary invasion by these organisms. As far as could be determined, no reports have been rendered on some of these dermatologic diseases. (The table shows that 47 patients were treated by local medication.) In most of these cases it was possible to identify an organism or the organisms which could be tested by biologic assay. The treatment consisted of application of wet dressings or ointment of tyrothricin. In the 7 patients with sycosis vulgaris who had previously been treated with roentgen therapy, vaccine and ointments the response was good and almost immediate. In all of the cases, however, tyrothricin failed to prevent recurrences. In 1 case, of several years' duration, wet dressings aggravated the eruption.

In the cases of pustular cystic acne in which *Staphylococcus aureus* was cultured little improvement resulted from the use of wet dressings and ointment containing tyrothricin. The wet dressings were applied three times daily. The ointment was applied at night. No permanent beneficial improvement resulted. The use of tyrothricin locally in this type of acne was of no avail.

Local treatment was used with dramatic results in 8 cases of impetigo contagiosa. Treatment consisted of application of wet dressings and tyrothricin ointment. In these cases *Staph. aureus* and *Streptococcus pyogenes* were recovered. Tyrothricin assay indicated that these organisms would respond promptly to such therapy. All of these cases responded on an average in six days.

In a group of 12 cases, 2 of which were cases of ecthyma from which *Staph. aureus* and beta hemolytic streptococci were recovered, wet dressings of tyrothricin gave temporary superficial improvement. Once crusts began to form tyrothricin failed to heal the lesion. In 4 cases of seborrheic dermatitis and 6 cases of fungous infection, which were obviously secondarily infected, decided improvement resulted from tyrothricin therapy. In those cases in which the hemolytic streptococcus could be recovered, the infection cleared promptly. Little effect was noted on the primary cutaneous disorder. In a small series of cases of variable eruptions, consisting of pyoderma, dermatitis repens, acrodermatitis perstans

*Results of Treatment with Tyrothricin in Patients with Various Cutaneous Diseases*

Name of Disease	Number of Cases	Average Duration	Smear and Culture	Tyrothricin Assay by Standard Serial Dilution Tests, Average %	Treatment	Results
Sycosis vulgaris	7	3 yr	Staph aureus Str pyogenes	0.06	Wet dressings, Ointment	Slight improvement in 6 No permanent benefit in 1
Acne (pustular)	5	1 yr	Staph aureus	0.03	Wet dressings, ointment	No improvement in 5
Impetigo contagiosa	8	5 days	Staph aureus Str pyogenes	0.03	Wet dressings, ointment	Cure in 8
Dermatitis seborrhoeica with secondary infection	4	2 yr	Staph aureus Str pyogenes Beta hemolytic streptococcus	0.03	Wet dressings	Improvement, primary condition unaffected in 4
Zethyma	2	9 mo	Staph aureus Str pyogenes Beta hemolytic streptococcus	0.01	Wet dressings	Improvement, primary condition unaffected in 2
Ungus (trichophyton) secondarily infected	6	1 mo	Staph aureus Str pyogenes Beta hemolytic streptococcus	0.03	Wet dressings	Improvement, primary condition unaffected in 6
Decubitus ulcer	5	1 mo	B pyocyanus B coli B proteus Str viridans	No effect with 1% except on streptococci which were inhibited with 0.5%	Wet dressings	Slight improvement
Pyoderma (children)	3	4 wk	Staph aureus	0.12	Wet dressings	Improvement in 4 days
Dermatitis repens	2		Staph aureus		Wet dressings	Improvement in 4 to 10 days
Acrodermatitis perstans	3		Staph aureus		Wet dressings, ointment	No improvement
Nummular eczema	2				Wet dressings ointment	No improvement

and nummular eczema, the results were of some value. Beneficial response was obtained in 3 cases of pyoderma and in 2 cases of dermatitis repens. Complete failure followed the use of tyrothricin for acrodermatitis perstans and nummular eczema.

A series of 5 cases of paraplegia were also studied. All of these patients had traumatic myelitis. Complicating their spinal injuries they had many decubitus ulcers of varying sizes. The usual location of the ulcer was about the sacrum. Other sites involved were the anterior crest of both ilia, the knees and the heels of both feet. Tyrothricin as a wet dressing was used in this group for a period of two to four weeks so that the ulcer could be prepared for plastic repair. Various organisms were recovered, among them *Bacillus pyocaneus*, *Bacillus coli*, *Strep. viridans* and *Bacillus proteus*. The results were irregular. The lesions did improve in appearance and in the disappearance of the foul exudate. Plastic surgery was made easier by preliminary applications of tyrothricin and wet dressings. This compared favorably with the results obtained by local penicillin therapy. In all cases further surgical intervention was required for the complete cure of the ulcer. Tyrothricin was found of some use in these cases. In no case did the ulcers become free of the organisms under this treatment.

#### COMMENT

Tyrothricin extract consists of at least two substances, gramicidin and tyrocidin. In vitro tyrothricin exhibits its effect primarily against gram-positive bacteria. A slight bactericidal action against gram-negative organisms also occurs. Gramicidin exerts its effect only on the gram-positive bacteria. Tyrocidin exhibits a bactericidal effect against both the gram-positive and the gram-negative organisms. Herrell and Heilman<sup>3</sup> used tyrothricin in the treatment of a few localized infections. Results were not completely satisfactory. Infection caused by hemolytic streptococci seemed to respond most readily. Our results were similar. In the eruptions that were secondarily infected with the hemolytic streptococci the response was good. Twelve patients with localized ulcers were studied by Rammelkamp<sup>4</sup> in 1942. Good results were obtained in 9 cases. The lesions became sterile after several days of treatment. Rankin<sup>5</sup> treated 6 patients with ulcers of the skin and had satisfactory results in 5. In our cases improvement occurred only in superficial lesions, such as those of impetigo contagiosa. Benefit was

3 Herrell, W. E., and Heilman, D. Experimental and Clinical Studies on Gramicidin, *J. Clin. Investigation* **20**: 583 (Sept.) 1941.

4 Rammelkamp, C. H. Use of Tyrothricin in the Treatment of Infections, *War Med.* **2**: 830 (Sept.) 1942.

5 Rankin, L. M. Use of Tyrothricin in Treatment of Ulcers of the Skin, *Am. J. Surg.* **65**: 391 (Sept.) 1944.

obtained in other diseases such as sycosis vulgaris, ecthyma and infected dermatoses. Complete cures were the exception. No patients with stasis ulcers were treated. The effectiveness of this form of therapy is modified by the presence of inhibiting substances such as pus, serum or gram-negative bacteria. The accessibility of the sensitive organism to the tyrothricin also influences its effect.

No serious toxic reactions were encountered following the clinical administration of tyrothricin in our cases. In only 2 cases was local discomfort noted after repeated wet dressings. In 4 cases a contact dermatitis developed following the use of the ointment. This was believed to be due to sodium ethyl mercurithiosalicylate 1:40,000 contained in the ointment, used as a preservative. One half of our patients were treated with the tyrothricin ointment to which the preservative was not added. No reaction appeared in these cases. The preservative did not seem to influence the stability or effectiveness of the ointment.

Biologic assay was carried out with the various organisms identified in the lesions. The organism employed as a standard was *Staphylococcus aureus* haemolyticus, which required 0.06 units of penicillin to inhibit its growth. Growth of the same organism was inhibited by 0.06 per cent of tyrothricin. The tyrothricin assay was performed by the standard serial dilution method. In several of the cases from which organisms were isolated dilute solutions less than that required for the inhibition of standard *Staph aureus* haemolyticus was found sufficiently effective. These tests in vitro indicate that at least gram-positive organisms respond rapidly, the gram-negative organisms were little affected. *B. proteus* and *B. pyocyaneus* which were isolated from the cases of decubitus ulcer failed to show any inhibition by the serial dilution method. In contrast, these cases showed that the clinical response was meager in comparison with that obtained in vitro. This was perhaps due to the inaccessibility of the pathologic process, which did not come in contact with the active antibiotic agent.

#### SUMMARY

Cutaneous lesions in 47 patients were treated by application of wet dressings and ointment containing tyrothricin. This drug was found to be effective in impetigo contagiosa, pyoderma and dermatitis repens, but of limited benefit in sycosis vulgaris, ecthyma, acrodermatitis perstans, nummular eczema and secondarily infected eruptions. Tyrothricin therapy in our opinion is of little practical value in the treatment of the ordinary diseases of the skin. Only superficial inflammatory eruptions may be adequately treated. Secondarily invaded eruptions may also respond, especially if caused by the staphylococcus or streptococcus.



# NEVUS FLAMMEUS WITH GLAUCOMA

MAJOR S GOLDBERG

MEDICAL CORPS ARMY OF THE UNITED STATES

GLAUCOMA associated with nevus flammeus has been described in ophthalmologic literature from time to time, but apparently little reference is made in dermatologic reviews

This report adds but 1 more case to a still relatively small series of reported cases. It is also intended to awaken interest in the dermatologist who has an opportunity to see many cases of facial nevi

## REPORT OF A CASE

A 24 year old master sergeant was admitted to a general hospital on Sept 17, 1942. Two months prior to admission he had appeared for a routine examination. He was found to have defective vision.

The patient stated that he had always been fond of hunting and in his "teens" was a good marksman. About 1939 (three years before admission) his aim became inaccurate because of blurred vision. In 1940 glasses were prescribed by a nonmedical refractionist. His vision apparently remained the same (symptomatically) and glasses were used only sporadically. No pain nor discomfort was ever present.

Physical examination revealed nothing significant except for the ocular defects and the nevus. The blood count and the results of urinalysis were normal. The serologic reaction for syphilis was negative. The nevus was a typical port wine mark involving the right side of the face, extending from the brow above the right eye (including the lids and over to the outer rim of the orbit) down to the upper lip. The conjunctiva was free of involvement. There were no deformities of the globe and no nevoid involvement.

Results of ocular examination were as follows: vision right 8/200 eccentric, left 20/20, normal conjunctivas and scleras, anterior chambers of equal depth, intraocular tension (MacLean) right 55 mm, left 32 mm, the right temporal field was limited to a temporal island abutting the fixation points and the left visual field and blindspots were normal, the right disk was deeply excavated and atrophic.

An attempt was made to reduce the pressure first with pilocarpine, then with physostigmine salicylate and alternating 2 per cent pilocarpine and 1 per cent physostigmine salicylate every hour. There was no demonstrable change in pressure. A sclerocorneal trephinement was performed on October 30. The post-operative course was uneventful.

The patient was last seen Dec 3, 1942. The vision was 15/200, and intraocular tension was normal. An attempt was made to follow the course of this patient, but follow-up records were not available. In a personal communication from the patient, no longer in the army, I was informed that he was under medical supervision and that the intraocular tension was below normal.

## COMMENT

The usual response of glaucoma to therapy is reported as unsatisfactory. No adequate appraisal of the surgical procedures in this case is warranted. The factors in the production of simple glaucoma associated with nevus flammeus are unknown and seem quite unrelated to those resulting in a buphthalmic eye.

Two publications are noteworthy for excellent reviews of the literature, one by A. J. Ballantyne,<sup>1</sup> of Glasgow, Scotland, and the other by O'Brien and Porter,<sup>2</sup> of Iowa City.

Schirmer<sup>3</sup> in 1860 was the first to report the association of glaucoma and nevus flammeus. It was not until 1879 that a second case was reported, by Sturge.<sup>4</sup> The literature has slowly increased until some 70 cases have been reported through 1944.

An interesting feature of this syndrome is the variegated ocular response—namely, nevus flammeus with buphthalmos, with simple glaucoma, with secondary glaucoma, with pseudoglaucoma and with cerebral disease.

The first reported case, that of Schirmer, was one of buphthalmos (infantile glaucoma) in which he described a capillary nevus affecting the skin of the face and trunk and the mucous membranes of the eye, nose, mouth and pharynx, associated with buphthalmos of the left eye. There was decided dilatation of the retinal veins. The case of Horrocks<sup>5</sup> was that of a 9 year old girl with a nevus of one side of the face, including the lids. The conjunctival and retinal vessels were dilated, and epileptiform convulsions of the opposite side were also noted. In the case of Sturge, glaucoma was present with a "port wine" mark of the face. It is not clear that this was a true buphthalmos. Epileptiform convulsions were also present.

In 1923 Duschnitz,<sup>6</sup> Salus,<sup>7</sup> Safar<sup>8</sup> and Lowenstein<sup>9</sup> reported cases of nevus flammeus associated with simple glaucoma. Salus reported 2

1 Ballantyne, A. J. Buphthalmos with Facial Naevus and Allied Conditions, *Brit J Ophth* **14** 481, 1930.

2 O'Brien, C. S., and Porter, W. C. Glaucoma and Naevus Flammeus, *Arch Ophth* **9** 715 (May) 1933.

3 Schirmer, R. Ein Fall von Teleangiectasie, *Arch f Ophth* **7** (pt 1) 119, 1860.

4 Sturge, W. A. A Case of Partial Epilepsy, Apparently Due to a Lesion of One of the Vaso-Motor Centres of the Brain, *Tr Clin Soc London* **12** 162, 1879.

5 Horrocks, P. A case of Facial and Ocular Naevus, *Tr Ophth Soc U Kingdom* **3** 106, 1883.

6 Duschnitz. Rechtseitiger Naevus flammeus mit Glaukom, abstracted, *Ztschr f Augenh* **50** 246, 1923.

7 Salus, R. Glaukom und Feuermal, *Klin Monatsbl f Augenh* **71** 305, 1923.

case of unilateral facial nevus with involvement of the conjunctivas and lids and with excavation of the disk on the same side

Duschnitz reported a case of similar involvement in an 11 year old girl. Thus these reports introduced a new aspect in showing that the glaucoma may come on later in life and may not be congenital.

The clinical picture of secondary glaucoma is derived from the presence of intraocular involvement. In the reported cases, there has been noted massive angioma of the choroid with or without retinal detachment or hemorrhages. Related to this syndrome is von Hippel's (Lindau's) syndrome through angiomatosis of the retina and the presence of congenital vascular disease of the nervous system.

Ballantyne in his review credited Sturge (1879) with relating the nevus condition of the vessels of the face to that of the brain. Cushing<sup>10</sup> expressed the opinion that the facial nevus has a tendency to follow along the course of the trigeminal nerve, and he was first to prove the presence of meningeal nevus. It is possible that the intraocular involvement of buphthalmos is similarly effected. In cases with attendant cerebral manifestations, roentgenography of the skull may reveal calcification. Calcification is not a constant finding, particularly if the case is observed early.

#### SUMMARY

From a review of the literature several features are revealed. Glaucoma is associated with facial nevus only if the nevus involves the lids or other ocular structures. 2. The causative factors in the production of glaucoma are not always the same. 3. Facial nevus is often associated with meningeal involvement and frequently follows distribution of the trigeminal nerve. 4. The glaucomatous process is usually of the infantile type (buphthalmos), but it may be a chronic simple glaucoma developing later in life.

8. Safar, K. Histologischer Beitrag zur Frage des ursachlichen Zusammenhanges zwischen Hydrophthalmus congenitus und Naevus flammeus, *Ztschr f Augenh* **51** 301, 1923.

9. Lowenstein, A. Aussprache, abstracted, *Klin Monatsbl f Augenh* **70** 540, 1923.

10. Cushing, H. Cases of Spontaneous Intracranial Hemorrhage Associated with Trigeminal Nevus, *J A M A* **47**:178 (July 21) 1906.

# Clinical Notes

## EXFOLIATIVE DERMATITIS ASSOCIATED WITH AMEBIC DYSENTERY

FRANK G WITHERSPOON, M D, ST -LOUIS

A patient with an exfoliative dermatitis of three years' duration was recently treated at the Barnard Free Skin and Cancer Hospital. During his stay at the hospital, it was discovered that he had an *Endamoeba histolytica* infection of the intestinal tract. Successful amebacidal therapy brought about a dramatic improvement in the eruption.

### REPORT OF A CASE

R C, a white farmer aged 54, was admitted to the Barnard Free Skin and Cancer Hospital on May 17, 1945 and discharged on July 16.

*History*—Three years prior to his present entry into the hospital, the patient had an eruption after he had sprayed tobacco with paris green. Although the patient had used no paris green since then, the eruption persisted. A year later a gastrointestinal disorder developed, during which time diarrhea, abdominal pain and bloody stools were present. Six months later (eighteen months after the onset of the eruption) the patient was first admitted to the Barnard Hospital, a roentgenologic examination of the gastrointestinal tract revealed no demonstrable lesions. Biopsy of a specimen from the rectum showed only chronic proctitis. At this time the dermatologic picture was one of contact dermatitis, with the face, neck, arms and trunk involved in a weeping eczematous eruption, but there was no exfoliation. The patient showed only slight improvement during hospitalization and was discharged after three weeks. The treatment during this hospitalization and subsequently while he was an outpatient consisted of routine palliative measures, soothing lotions and starch baths. No benefit was derived from this therapy, and the patient's condition grew steadily worse.

On his recent admission, the eruption had developed into an exfoliative dermatitis. For several months flaking and scaling of the skin had been present. This condition had become worse until a generalized exfoliation was present, with a weeping eczematous eruption of the extremities. Pruritus became intense, and sleep was virtually impossible. He had lost 35 pounds (16 Kg) in recent months.

*Examination*—The patient was a fairly well developed but poorly nourished man. His skin was wrinkled and lichenified. Exfoliation was general but greatest on the face and extremities. A weeping eczematous eruption of the forearms, inguinal region and legs was present. The hands were hyperkeratotic, and deep fissures were present on the joints of several fingers. The dorsa of the feet were fissured. Small areas of leukoplakia were present in the mouth, and the teeth were carious. The heart was slightly enlarged, and the blood pressure was 155 systolic and 105 diastolic. There was some tenderness on palpation of the abdomen in the umbilical region and in the left lower quadrant. Several large hemorrhoids

Studies, observations and reports from the Department of Dermatology of the Barnard Free Skin and Cancer Hospital and the Department of Dermatology, Washington University School of Medicine, Service of Dr M F Engman Sr

were present, and the prostate gland was hard and slightly enlarged. A small hernia was present in the right inguinal region.

*Laboratory Data*—The urine was normal, and serologic reactions were negative on admission. The hematologic findings on May 17, 1945 were as follows: hemoglobin, 69 per cent, red blood cells, 3,110,000 per cubic millimeter, and white blood cells, 19,600, with 42 per cent segmented polymorphonuclear leukocytes, 22 per cent nonsegmented polymorphonuclear leukocytes, 10 per cent eosinophils, 2 per cent basophils and 24 per cent lymphocytes. On June 8, 1945 the stool contained motile forms of *E. histolytica* and on June 23 no organisms. Prior to this, two gastrointestinal roentgen ray examinations revealed normal conditions. On July 4, 1945, an examination of the blood showed hemoglobin, 78 per cent, red blood cells, 4,650,000, and white blood cells, 7,750, with 70 per cent segmented polymorphonuclear leukocytes, 4 per cent nonsegmented polymorphonuclear leukocytes, 2 per cent basophils, 22 per cent lymphocytes and 2 per cent monocytes.

*Treatment*—Daily starch baths and various lotions were used with little success for two and one-half weeks. When amebiasis was discovered, treatment was begun with emetine hydrochloride, 1 grain (0.06 Gm) daily, hypodermically, and chiniofon, in doses of 4 grains (0.26 Gm) three times a day, the drugs being given concurrently. This dosage was maintained for ten days. The diarrhea had ceased by the end of the third day of treatment, and the abdominal symptoms disappeared before the end of ten days. The pruritus decreased gradually, and gain in weight progressed rapidly. In six weeks 20 pounds (9 Kg) had been gained, and the dermatitis has practically disappeared. During this time only starch baths and soothing lotions were given, such as had been used for some eighteen months without success.

#### COMMENT

It seems significant that a severe chronic dermatitis should yield to no treatment for three years and then show a 90 per cent improvement in six weeks when amebiasis was discovered and properly treated. Although eosinophilia is not commonly associated with amebic infection, the blood picture showed 10 per cent eosinophils on the admission of the patient. This percentage dropped to zero after successful therapy of the amebiasis.

#### SUMMARY

A case of exfoliative dermatitis with an associated amebic dysentery is described. On successful treatment of the amebic infection great improvement in the dermatologic condition occurred. A search of the available literature has revealed no similar case.

### TREATMENT OF VARICOSE ULCERS WITH SILVER-COATED ADHESIVE TAPE

FRITZ B. REIF, M.D. NIAGARA FALLS, N. Y.

The use of silver foil in the treatment of varicose ulcers was first recommended by Ludwig Isaak (*Dermat Wchschr* 92:807 [May 30] 1931). In his paper on effective treatment of various ulcers of the leg (*ARCH DERMAT & SYPH* 41:530 [March] 1940) Isaak again described his technique. After the surrounding skin is protected with a thick layer of paste of zinc oxide the ulcer is covered with a few layers of thin genuine silver leaf and then with a thick layer of cotton

and bandaged tightly To my knowledge, no further publications on the use of silver foil have appeared since

The main reason that this method did not meet with the approval which it deserves seems to be the difficulty in handling the very thin and easily torn foil The Duke Laboratories distributed a silver foil on a rigid pink cloth backing (Argentoplast, Beiersdorf), but their supply was exhausted long ago

After some experiments with other material I found the following method simple and satisfactory

A piece of adhesive tape—for larger ulcers strips of adhesive tape—slightly larger than the ulcer is pressed onto the silver foil, which sticks to the tape The silver foil is then cut along the edges of the adhesive tape, and the silver-coated tape is placed over the sore It is reenforced with more layers of plain adhesive tape to exert the necessary pressure For ulcers with much discharge I cover the surrounding skin with paste of zinc oxide (as done by Isaak) or with petrolatum The adhesive tape is covered with a gauze pad and absorbent cotton and kept in place by means of a tight bandage The leg up to the knee is supported by an elastic bandage (Tensor bandage)

It is well known that the genuine metallic silver has a bactericidal effect Laboratory tests with the silver foil I used did not show any bacterial growth

Slight maceration of the skin by the discharge which occasionally occurs is easily controlled with wet dressings, preferably with a silver nitrate solution (1 1,000), applied for a twenty-four hour period

The method may be useful not only in the treatment of varicose ulcers but also for the stimulation of growth of granulation tissue and of epithelial cells in slowly healing wounds

Pine and Main streets

# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

ROENTGEN THERAPY OF BOECK'S SARCOID ERNST A POHLE, LESTER W PAUL and ELIZABETH A CLARK, Am J M Sc 209 503 (April) 1945

Pohle and his associates point out the conflicting nature of reported opinions as to the effectiveness of roentgen radiation for various manifestations of sarcoid, and they record their own experiences. Fourteen patients have been treated by roentgen rays in the Department of Radiology at the State of Wisconsin General Hospital for lesions of Boeck's sarcoid on the chest, 8 of these have been observed sufficiently long to warrant certain preliminary conclusions. Within the period of observation, 6 of the 8 have shown definite roentgenologic evidence of improvement.

THE TREATMENT OF TULAREMIA WITH INTRAVENOUS BISMUTH SODIUM TARTRATE WILL W JACKSON, Am J M Sc 209 513 (April) 1945

Sixty-one consecutive cases of tularemia of various types are reported, all patients recovered promptly after intravenous injections of a solution of bismuth sodium tartrate especially prepared for intravenous application. (Jackson reports that he has given ninety thousand intravenous injections of bismuth without serious reaction.) The author emphasizes the benefit from prompt initiation of therapy, even before the diagnosis has been confirmed by laboratory examinations.

A CLINICAL STUDY OF SENSITIVITY TO SULFATHIAZOLE GERALD T KENT and HERBERT W DIEFENDORF, Am J M Sc 209 640 (May) 1945

Untoward reactions were observed in 110 patients among the 472 to whom sulfathiazole was administered for the first time (approximately half of these had allergic reactions). Slightly more than 3 per cent of the whole group presented cutaneous reactions, usually a generalized eruption but occasionally erythema nodosum. Sulfathiazole was readministered to 103 patients, and it was given a third time to a few patients. In 22 of the group to whom sulfathiazole had been readministered "allergic reactions" developed. Two of these had cutaneous reactions in addition to "drug fever" on first administration but on readministration had only the fever without cutaneous reaction. Two patients had cutaneous reactions to the second administration though the first administration had been well tolerated. In 1 patient to whom the drug was administered on three occasions the last administration resulted in a cutaneous reaction, conjunctivitis and nephrosis.

Kent and Diefendorf state that if a patient has had no reaction after nine days of therapy, his chances of having one subsequently on the same administration diminish rapidly. Reactions to the second administration of sulfathiazole are likely to occur within the first two days if a reaction occurs in the first course, or after nine days if the first course had been well tolerated.

INITIAL CARDIAC EXAMINATION OF 23,000 INDUCTEES AND VOLUNTEERS NATHAN FLAXMAN, Am J M Sc 209 657 (May) 1945

Flaxman examined 23,000 men between the ages of 17 and 38 years, of whom 1,621 (7.4 per cent) gave a history or had the physical signs of heart disease, only 226 (1 per cent) of the total group examined had organic heart disease, however, and only 3 of them (Negroes) had syphilitic aortic insufficiency. Flaxman was impressed by this extremely low incidence of syphilitic heart disease, he believes it can be explained only by the excellent treatment that most syphilitic persons receive, based on the modern public health program.

ACUTE SYPHILITIC MENINGITIS A DISCUSSION OF THE PROBLEMS ENCOUNTERED  
IN THE DIAGNOSIS ALBERT HEYMAN, *Am J M Sc* **209** 664 (May) 1945

During a period of two years Heyman observed 9 cases of acute syphilitic meningitis, 5 of which presented diagnostic difficulties. The observed manifestations in the cases fell into three rather sharply delineated groups: (1) basilar meningeal signs (predominantly cranial nerve palsies), (2) symptoms referable to the cerebral vertex, and (3) signs of acute hydrocephalus.

In 2 instances the symptoms developed while the patient was receiving treatment with bismuth preparations (one received it in the form of a soluble salt at weekly intervals).

Response to treatment is not always satisfactory evidence of a correct diagnosis. Not only will syphilitic meningitis frequently improve without treatment, but other types of lymphocytic meningitis may get well coincidentally with anti-syphilitic treatment. Heyman states that since syphilitic meningitis is not a rapidly fatal condition, it seems advisable to withhold treatment in cases of undiagnosed lymphocytic meningitis, unless the patient is very ill, in which case a therapeutic trial with oxophenarsine hydrochloride is justified.

According to Heyman, not only are false positive Wassermann reactions elicited in the spinal fluids of patients with nonsyphilitic meningitis, but occasionally false negative reactions occur in patients with syphilitic meningitis. When the diagnosis is suspected but the Wassermann reaction is negative, Heyman advises withholding treatment in order to establish a definite diagnosis of syphilitic meningitis.

PRIMARY SYSTEMIC AMYLOIDOSIS STUART LINDSAY and WILLIAM F KNORP,  
*Arch Path* **39** 315 (May) 1945 PRIMARY SYSTEMIC AMYLOIDOSIS OF THE  
ALIMENTARY TRACT ABNER GOLDEN, *Arch Int Med* **75** 413 (June) 1945

In the case reported on by Golden a patient with primary systemic amyloidosis presented a bright red, glossy tongue, in the case described by Lindsay and Knorp there was involvement of the nasal mucosa, with hemorrhage, septal perforation and bilateral nasal obstruction. Both reviews mention the frequency with which primary systemic amyloidosis involves the mucous membranes and the skin.

LYNCH, St Paul

EFFECT OF MALARIA ON SEROLOGIC TESTS FOR SYPHILIS ARTHUR A ROSENBERG,  
*Bull U S Army M Dept*, January 1945, no 84, p 74

The investigation was undertaken at a large army hospital where many cases of malaria were available for study, with the purposes of determining which of the serologic tests gave the least proportion of false positive reactions and whether it was possible to distinguish malaria from syphilis on the basis of definite patterns of positivity among the different tests. The standard flocculation tests described by Kahn, Mazzini, Eagle, Hinton and Kline and the standard complement fixation test of Kolmer were employed in this study. More than 8,000 serologic tests were performed on patients whose histories contained no evidence of syphilitic infection but who had malaria.

The following observations were made. The Mazzini test elicited 51 per cent false positive reactions, the Kahn test 47.5 per cent, the Kline test 33.6 per cent, the Kolmer test 20.4 per cent, the Eagle test 10.4 per cent and the Hinton test 5.8 per cent.

The author concludes that the pattern of positivity for malaria is: positive reaction to the Kahn and Mazzini tests, doubtful reactions to the Kolmer and Kline tests and negative reactions to the Eagle and Hinton tests.

VERIFICATION TESTS IN SERODIAGNOSIS OF SYPHILIS CHARLES R REIN and  
GEORGE R CALLENDER, *Bull U S Army M Dept*, February 1945, no 85, p 108

The authors discuss the limitations of verification tests in the serodiagnosis of syphilis. They point out that before any test can be considered of practical value



as a verification procedure and used routinely it must be able to satisfy the following criteria 1 Serums from syphilitic persons with positive serologic reactions should always give a syphilitic type of verification reaction No test at the present time satisfies this criterion 2 Serums from nonsyphilitic persons with positive serologic reactions should always give the false positive type of verification reaction This too, is not fulfilled by any of the present verification tests 3 The diagnosis of syphilis should be established for persons who consistently give the syphilitic types of verification reaction on repeated examination 4 The diagnosis of syphilis should be excluded for persons who consistently give the biologic false positive (nonsyphilitic) type of verification reaction on repeated examination

Rein and Callender concluded that in questionable cases, those persons in whom there is no clinical or anamnestic evidence of syphilis but who have had doubtful or positive serologic reactions on repeated occasions, the various verification tests proved to be of no value

STRAKOSCH, Denver

TREATMENT OF URTICARIA WITH SYNTHETIC VITAMIN K J H BLACK, J Allergy  
16 83 (March) 1945

The author administered 2 mg of an analogue of vitamin K three times daily to 156 patients suffering from chronic urticaria In each of these cases the usual methods of investigation and treatment, including scratch and intradermal tests, trial diets, search for infections and avoidance of drugs, had failed to bring about relief

Most of the patients were young and middle-aged adults The duration of the disease varied from one month to twenty years

The preparation used was menadione (2-methyl-1,4-naphthoquinone), an analogue of vitamin K

The results were gratifying, relief was obtained in approximately 62 per cent of the cases after one to four weeks' treatment In many instances lesions failed to appear after two days of treatment In 28 patients (31 per cent) there was a relapse Readministration of the vitamin brought about prompt relief in each instance No second recurrence was observed in any patient

Determinations of prothrombin time were performed for 119 patients Clotting within twenty-five to thirty seconds was considered normal The prothrombin time was normal in 41 patients and prolonged in 78 patients Relief from chronic urticaria was obtained in 78 per cent of the patients with prolonged time and only in 32.5 per cent of those with normal time

MENDELSON, New York

THERAPEUTIC EFFECTIVENESS OF PENICILLIN IN THE TREATMENT OF VINCENT'S STOMATITIS AND ITS FAILURE TO INFLUENCE FAVORABLY CERTAIN OTHER MEDICAL CONDITIONS JAMES S SWEENEY, WILLIAM J MORGINSON, ROGER W ROBINSON and ELMER M KILPATRICK, J Lab & Clin Med 30 132 (Feb) 1945

Forty-three patients with Vincent's stomatitis were treated with the antibiotic penicillin, with good results The penicillin was administered intramuscularly in doses of 25,000 units every three hours After forty-eight hours it was impossible to find fusiform bacilli or spirochetes except in patients in whom dental caries existed These organisms rapidly disappeared after dental prophylaxis There was an increase in temperature from 99.1 to 101 F during the time the penicillin was administered The results obtained from the use of penicillin in other conditions were as follows

1 In 3 cases of chronic recurring furunculosis the treatment was regarded only as palliative or as a temporary adjunct, for there were recurrences

2 In 11 cases of acne vulgaris, there were some signs of improvement, but none of the patients were cured and there was no decided improvement

3 In 7 cases of staphylococcic dermatitis there was some evidence of improvement, but relapse was frequent

4 In 7 cases of asthma due to various strains of staphylococci and streptococci recovered from the paranasal sinuses there was some initial improvement but it was not sustained

5 In 5 cases of malaria there was no improvement from the treatment. However, the patients when subsequently treated with small doses of antimalarial agents responded promptly. There were no recurrences of malaria at the end of six months

6 In 2 cases of subacute bacterial endocarditis the cultures of the blood became sterile during the treatment but they became positive for pathogens after the treatment was stopped

7 In 1 case of acute disseminated lupus erythematosus there was no clinical improvement at any time during the treatment

8 One or more patients with the following diseases failed to respond to the administration of penicillin: chronic pyelonephritis, aerobic and anaerobic non-hemolytic streptococcus infections, diphtheria, mumps, eczema, folliculitis, dermatitis herpetiformis, acute myeloid leukemia and follicular lymphoblastoma (Brill-Symmers disease). There were several patients with trichophytosis who showed no improvement during administration of penicillin. Three patients showed mild to moderate urticarial reaction from the treatment, this disappeared within a few days during the period of penicillin therapy

**SIMPLE TECHNIQUE FOR ESTIMATION OF PENICILLIN IN BLOOD AND OTHER BODY FLUIDS** MARY B WOLOHAN, WINDSOR C CUTTING and MARY W CUTTING, *J Lab & Clin Med* **30** 161, 1945

While the Oxford cup method for the assaying of penicillin is applicable to fluids containing a high concentration of the drug, it is unsatisfactory for clinical determination in the blood, in which the concentration is usually less than 1 unit per cubic centimeter

The authors found that a simplification of the Fleming method (Herrell, of Mayo) for the estimation of penicillin in the blood was less laborious than the commonly used Rammelkamp method. The three methods are basically similar. Each consists of a serial dilution of the unknown blood and the addition of a constant inoculum of hemolytic streptococci. After incubation the tubes are observed for evidence of inhibition of growth of the bacteria and compared with controls, similarly prepared but containing known amounts of penicillin. Wolohan and her associates compared the penicillin content of blood from man, dog and rabbit containing variously from 0.01 to 4 units per cubic centimeter and found the results in accord.

The technic of test is discussed in detail. The simplification of the procedure depends on the elimination of centrifugation of the blood specimen, the addition of a known amount of blood and the use of capillary tubes (Kimble Brand 34500).

This method can be used in determining the concentration of penicillin in other body fluids

GELBER, Los Angeles

**ECTHYMA TEREBRANT (A RARE FORM OF TUBERCULID)** PAUL POIRER, *Union med du Canada* **74** 32 (Jan) 1945

The author reports the case of a 21 year old man who presented an eruption on the face, neck, and back, made up of comedos, papules, pustules, scars and deep indolent ulcers (acne conglobata?). Tuberculoid structure was noted microscopically, and apparently because of this the author felt that the disease was a tuberculid. The reaction to a Vollmer patch test with tuberculin was negative, and tubercle bacilli could not be found. Roentgen irradiation produced healing in four months.

SPRING AND SUMMER DERMATOSES HENRI SMITH, Union med du Canada  
74 756 (June) 1945

Dermatoses are called seasonal if they occur or relapse with increased frequency at a certain time of year. Spring and summer dermatoses can be divided into five groups: (1) eruptions, such as erythema multiforme, which are seasonal for unknown reasons, (2) those which are aggravated by atmospheric conditions of spring and summer (heat and humidity), such as dermatophytosis and plant dermatitis, (3) lesions, such as insect bites, which occur only during the warm months, (4) sudoral eruptions, such as miliaria, and (5) eruptions caused directly or indirectly by exposure to sunlight.

In the first group Smith includes and briefly discusses erythema multiforme, erythema nodosum, pityriasis rosea, recurrent herpes, vitiligo and tinea versicolor.

Among dermatoses aggravated by heat and humidity are listed symmetric lividity of the soles, "athletes foot" and contact dermatitis due to footwear.

Regarding ivy dermatitis the author recommends injections of an alcoholic extract of the plant, stating that of 1,851 patients so treated 86.4 per cent were greatly benefited and only 2.1 per cent had aggravations of the eruptions. He believes that similar injections are more useful prophylactically than is oral therapy.

Sunburn, freckles, dermatitis and prurigo aestivalis are also discussed. Smith is pessimistic concerning therapeutic methods used to reduce photosensitivity. Xeroderma pigmentosum, hydroa vacciniforme, pellagra, cheilitis solaris, berlock dermatitis and dermatitis due to meadow grass are also placed in the group of eruptions influenced by sunlight. Photosensitivity produced by drugs is mentioned, and it is the author's opinion that sulfonamide compounds should never be used topically.

LAYMON, Minneapolis

PENICILLIN A PROGRESS REPORT BASED ON 1,455 CASES TREATED AT THE  
NATIONAL NAVAL MEDICAL CENTER, BETHESDA, MARYLAND, U S Nav M  
Bull 44 453 (March) 1945

A section of the report of the Penicillin Committee of the National Medical Center deals with results in the treatment of syphilis and various cutaneous diseases.

Of a total of 324 patients treated for syphilis, the disease was in its early stages in 250 and in the remainder the disease was either in a latent stage or involved the central nervous system. An analysis made after cessation of treatment revealed that of the patients in whom syphilis was in its early stages 237 remained free of symptoms, 7 had clinical or serologic relapses and 6 contracted new infections.

The patients were routinely treated as follows: (1) early syphilis—10,000 units every three hours for sixty doses (a total of 2,400,000 units in seven and one-half days), (2) latent syphilis—10,000 units every three hours for one hundred doses (a total of 40,000,000 units in twelve and one-half days) and (3) central nervous system syphilis—40,000 units every three hours for two hundred doses (a total of 8,000,000 units in twenty-five days) followed by ten units of artificial fever and ten accompanying injections of 60,000 units each. The committee felt that penicillin was the best drug ever made available for treatment of syphilis because it produced (1) rapid disappearance of the organism, (2) rapid healing of gummas and (3) a quick reversal of serologic reactions of the blood and spinal fluid. Furthermore, it was safer and better tolerated than other antisyphilitic medicaments.

About 200 patients were treated with penicillin locally or systemically for various cutaneous diseases. The pyodermas when caused by susceptible organisms respond well to treatment. Furunculosis was controlled temporarily. Failures were recorded in treatment of pustular acne, erythema multiforme, mycosis fungoides, dermatitis herpetiformis, eczema, fungous infections and scabies.

RODIN, South Bend, Ind

# Society Transactions

## MINNESOTA DERMATOLOGICAL SOCIETY

S E Sweitzer, M D, *President*

H A Cumming, M D, *Secretary*

*Minneapolis, Nov 3, 1944*

### A Case for Diagnosis (Necrobiosis Lipoidica?) Presented by DR JOHN F MADDEN, St Paul

Mrs F F, a housewife aged 53, was presented at the October 1943 meeting of the Minnesota Dermatological Society. The patient has had recurrent ulcers involving the entire legs from knees to ankles for the past seven years. The ulcers are healed at this time. She has had ligations of the bilateral saphenous vein and many injections for varicose veins. The patient is 5 feet 5 inches (165 cm) tall and weighs 300 pounds (136 Gm). She has irregular asymptomatic plaques with orange yellow borders and light pink centers extending from the lower third of the thighs to the ankles. None of the lesions are ulcerated. The urinalysis showed a sugar content as high as 4.8 per cent in 1943. The urine is now free of sugar. The fasting blood sugar has ranged from 150 to 350 mg per hundred cubic centimeters. The fasting glucose tolerance test showed 143 mg per hundred cubic centimeters, 253 mg at the end of the first hour and 246 mg at the end of the second hour. There was no sugar in the urine at that time, and the patient was considered to have a high renal threshold. The blood urea nitrogen was 15.4 mg per hundred cubic centimeters. A roentgenogram showed extensive calcification of the blood vessels of the legs. The medical staff does not feel that the patient has diabetes mellitus. They seem to think that she has some type of glandular dysfunction.

#### DISCUSSION

DR FRANCIS LYNCH, St Paul. Though the patient does not have diabetes, she does have some disturbance of glucose and lipid metabolism. She also has syphilis, which is apparently unrelated to the present condition. She stated that she had had varicose veins, static ulcers and dermatitis, but this part of her history is not clear. None of these factors seems to offer a satisfactory explanation for the present eruption, and the section does not show necrobiosis. I think that she has a lipid deposit in and around scar tissue, with cutaneous changes due to some systemic disease, whose nature is vague.

DR JOHN F MADDEN, St Paul. I think that Dr Lynch's remarks explain what is seen. Dr O'Leary said that the eruption was probably originally on the basis of a deeply situated vasculitis involving perhaps the veins and maybe the arteries in the legs.

DR S E SWEITZER, Minneapolis. There is no edema, just fibrosis.

DR JOHN F MADDEN, St Paul. For years she had large varicose veins, and roentgenograms now show extensive calcification of the superficial vessels.

### Necrobiosis Lipoidica Presented by DR JOHN F MADDEN, St Paul

Mrs J P M, a housewife aged 35, stated that asymptomatic reddish yellow plaques began to appear on the anterior surfaces of both legs during 1943. New plaques continued to appear from time to time. At present, the greater part of the shins is covered with irregular lesions from the knees to the ankles. The largest

plaque is about 6 inches (151 cm) long and 2 inches (5 cm) wide. The lesions are elevated, firm and painless and are of an orange yellow color at the periphery, changing to varying shades of pink as the centers are approached. The fasting blood sugar was 100 mg per hundred cubic centimeters. The urine gave a negative reaction for sugar on several occasions. The patient has no knowledge of ever having had diabetes mellitus. The Wassermann reaction of the blood was negative.

## DISCUSSION

There was no discussion of this case.

### Necrobiosis Lipoidica Diabeticorum Presented by DR FRANCIS LYNCH, St Paul

Miss A G O, 18 years, noted a lesion on the left leg nearly two years ago, following an injury. The lesion has gradually enlarged. The patient has been known to be diabetic since the age of 9 years and has taken insulin fairly regularly, though not under medical supervision in recent months. On the left anterior tibial surface is a slightly yellow-red, smooth, oval lesion about 2 inches (5 cm) in length, with a red border. The skin is atrophic, and a few vessels are visible on the surface.

## DISCUSSION

There was no discussion of this case.

### Pseudopelade Presented by DR JOHN F MADDEN, St Paul

H L, a laborer aged 32, stated that he noticed small, pea-sized patches of alopecia appearing over the frontal portion of his scalp in 1943. There were no signs of inflammation. The eruption was asymptomatic, and hair did not regrow in any of the patches. The disease progressed steadily since its onset. The eruption now covers most of the scalp but is more extensive on the frontal portion and crown. The lesions are round, white, shiny scars, the size of beans or peas, scattered in the aforementioned areas. The Wassermann reaction was negative.

## DISCUSSION

There was no discussion of this case.

### Pseudopelade Presented by DR JOHN F MADDEN, St Paul

Mrs R A, a housewife aged 56, states that she began to lose hair on the front of the scalp in 1941. There has been no eruption at any time, and there was no preceding illness. The loss of hair now involves most of the scalp, however, it is greatest on the frontal part and the crown. The scalp is covered with pea-sized to dime-sized atrophic scars, with apparently normal scalp and hair between the scars. The Wassermann reaction was negative.

## DISCUSSION

There was no discussion of this case.

### Keratodermatitis Hypoestrogenica? Presented by DR CARL LAYMON, Minneapolis

Miss L S is a white woman aged 42. An eruption on her soles developed in the late summer of 1943. Since Aug 7, 1944, when first seen, she has had diethylstilbestrol continuously (1 mg daily) and injections of estrone weekly. After four weekly fractional roentgenologic treatments during August 1944, her treatment with estrogenic substances was continued only for a period of two months, during which the lesions became much worse. In 1938 the patient had some pelvic operation, probably removal of fibromas of the uterus. The patient has had only two menstrual periods since that time.

There are thickened, fissured, keratotic, yellowish orange, sharply demarcated patches on both soles. There is an area relatively free of lesions in the central part of each sole. The lesions extend up on the sides of the heels and also involve the dorsal surfaces of the toes.

## DISCUSSION

DR S E SWEITZER, Minneapolis. In this case of keratodermitis hypoeestrogenica, there is apparently no improvement with treatment with diethylstilbestrol. Dr Laymon, has the condition improved at all?

DR CARL LAYMON, Minneapolis. The amount of improvement has certainly been slight.

DR FRANCIS LANCH, St Paul. In spite of the failure to respond to treatment, the eruption is characteristic of the type seen with estrogenic deficiency. Perhaps treatment has been inadequate. Since there have been no signs of overdosage, I suggest a trial of considerably larger daily amounts and perhaps a change from synthetic to natural estrogens.

**Tinea Capitis** Presented by DR JOHN F MADDEN, St Paul

The mother of L J B, a school boy aged 8, noticed that he began to lose his hair in August 1944. There are patches devoid of hair varying in size from that of a pea to that of a silver dollar. The hair in the lesions is broken off or absent. The lesions are scaly, but there is no evidence of exudation. He has three brothers and two sisters who have similar eruptions. This is one of approximately thirty children with ringworm of the scalp seen in St Paul during the past three years. Infections with *Microsporon lanosum* and *Microsporon audouinii* have been identified in various patients by cultures.

## DISCUSSION

DR JOHN F MADDEN, St Paul. These are some of the many cases seen during the past three years. We are trying to get cooperation from the school and city health authorities, without much success.

DR STEPHAN EPSTEIN, Marshfield, Wis. I have seen only 2 cases of tinea capitis due to *microsporon fungi* in Marshfield in recent months. I am somewhat hesitant to use thallium acetate for epilation of older children because I once encountered a severe, though nonfatal, reaction. For patients below 7 or 8 years, however, thallium acetate is relatively safe, and beyond that age there is no difficulty with roentgenologic epilation.

**A Case for Diagnosis** Presented by DR JOHN MADDEN, St Paul

Miss L S, aged 18, stated that a pimple appeared on the buttocks to the right of the gluteal cleft about September 1943. This lesion ruptured spontaneously, and the purulent contents were discharged. The lesion healed and recurred during the winter of 1944. It would rupture at intervals and discharge purulent fluid. The lesion was excised in August 1944, and there was a recurrence by October 1944. At present there is an irregular olive-sized erythematous, infiltrated plaque on the right side of the buttocks. The center is covered by a crust, and it is comparatively painless on manipulation. The patient has scars on the legs, which might be the result of erythema induratum. She also has an arrested widespread pulmonary tuberculosis.

## DISCUSSION

DR STEPHAN EPSTEIN, Marshfield, Wis. This girl has tuberculosis of the lungs and erythema induratum. I am familiar with such abscesses, starting around the rectum and perforating outside with sinuses. I have seen a number of them recur time and again, even with treatment of the rectum. The histologic

picture of nonspecific inflammation plus giant cells, I think, would fit in with the assumption that it is a tuberculous process

Dr S E SWEITZER, Minneapolis What would you advise?

Dr STEPHAN EPSTEIN, Marshfield, Wis I advise deep roentgen therapy, in some cases there is good response

Dr FRANCIS LYNCH, St Paul Rather than tuberculosis, could this be inflammation associated with a sinus tract from a pilonidal cyst? The patient has a tiny dimple at the tip of the sacrum

#### Epidermolysis Bullosa with Palmar and Plantar Keratosis and Verrucous Lesions at Sites of Previous Lesions Presented by Dr FRANCIS LYNCH, St Paul

Mr E K, 22 years of age, has had a generalized eruption present practically constantly since birth It is worse in summer The family history is negative for any type of eruption The teeth are said to have been normal in shape, but they were removed three years ago In recent years, warty lesions have appeared at the sites of many blisters There is an extensive eruption consisting of a moderate number of bullae, many discolored areas where there were formerly blisters and many verrucous papules also at the sites of former blisters The mouth shows pale areas of thickening at the sites of former lesions The palm of the left hand and the soles present diffuse yellow scaling and thickening

#### DISCUSSION

There was no discussion of this case

#### Granuloma Annulare Presented by Dr FRANCIS LYNCH, St Paul

E L H, a white woman aged 22, was first seen in October 1944, with an eruption on the dorsum of the left hand of eight years' duration and on the dorsa of the feet of four years' duration The patient stated that there has been no change in the appearance of the eruption from its onset until now Serologic reactions for syphilis were negative The Mantoux reaction was negative until six weeks after her field training (nursing) at a sanatorium

Examination shows numerous lesions on the dorsum of the left hand and the dorsa of both feet\* The right hand is free (the patient is left handed) The lesions are light brown and mostly papular, with the smaller ones 1/6 to 1/8 inch (0.4 to 0.3 cm) in diameter The larger papules show a slight central depression, and there are many rings 1/4 to 1/2 inch (0.6 to 1.2 cm) in diameter made up of papules of the same nature

Histologic section shows changes compatible with granuloma annulare

#### DISCUSSION

There was no discussion of this case

#### Nonsuppurative Panniculitis Presented by Dr JOHN MADDEF, St Paul

Mrs H D, a nurse aged 45, stated that deep-seated, painful nodules began to appear on various parts of the body in 1942 She now has approximately twenty deep-seated, painful olive-sized to pigeon egg-sized nodules on the shoulders and the arms and an occasional lesion on the trunk The nodules can be moved rather freely under the skin The newer lesions are more painful on manipulation There is no change in the color of the overlying skin

#### DISCUSSION

Dr JOHN MADDEF, St Paul I never thought of trying penicillin

Dr S E SWEITZER, Minneapolis Try it to see if it has any effect

**A Case for Diagnosis (Purpuric Lichenoid Dermatitis, Schamberg's Disease?)** Presented by DR JOHN MADDEN, St Paul

Mrs H M H, a housewife aged 48, stated that cayenne-pepper-like patches, varying in size from that of a dime to that of a silver dollar, began to appear on both legs during 1943. These were accompanied with slight itching. The old lesions grew in size and did not disappear. New lesions have continued to appear at intervals. There are no demonstrable varicose veins.

## DISCUSSION

DR L H WINER, Minneapolis. At the Minneapolis General Hospital and at the University of Minnesota Medical School, there are 2 patients with Schamberg's disease. Both patients were presented at various meetings with diagnoses of capillaritis with involvement of forearms and legs. Microscopic sections stained for iron showed the cutis loaded with iron. In this case, although the eruption has the clinical appearance of Schamberg's disease, there is not the great amount of iron seen in the histologic section of Schamberg's disease. Dermatologists have been prone to apply the term "Schamberg's disease" to all cases of stasis dermatitis localized only to the lower extremities and especially to areas where there are varicosities.

**Lichen Sclerosus et Atrophicus** Presented by DR JOHN MADDEN, St Paul

Mrs M M, a housewife aged 40, stated that she noticed an irregular, olive-sized lesion appearing on the left side of the neck about two years ago. This has grown slightly. It is asymptomatic, and there are no other lesions on the cutaneous surface. The eruption consists of the one irregular, white atrophic plaque with comedo-like plugs throughout.

## DISCUSSION

There was no discussion of this case.

**Sarcoidosis** Presented by DR JOHN MADDEN, St Paul

Mrs V H, a defense worker aged 30, was a ward attendant in the tuberculosis wards at the Ancker Hospital from 1936 to 1943. In 1943 an itchy, painless, marble-sized nodule appeared on the lateral surface of the left arm. This has not changed in size or appearance up to the present time. The lesion is a dully erythematous, painless, freely movable nodule on the lateral surface of the middle third of the right arm. The reaction to the Mantoux test was strongly positive. A roentgenogram of the chest showed no evidence of pulmonary tuberculosis.

## DISCUSSION

DR JOHN MADDEN, St Paul. Roentgenograms of the chest and bones showed no abnormality. It is interesting to note that the patient was a ward maid in the tuberculosis wards for about eight years.

**Glossitis Rhombica Mediana?** Presented by DR JOHN MADDEN, St Paul

Mrs N A W, aged 74, has a smooth red olive-sized asymptomatic plaque on the dorsal surface of the middle third of the tongue in the midline. It is of unknown duration.

## DISCUSSION

There was no discussion of this case.

**Trichotillomania** Presented by DR H E MICHELSON, Minneapolis

Mrs F B, a white woman aged 47, was seen in the outpatient department of the University Hospitals July 12, 1943, complaining of short, broken-off and colored (red, green and blue) hair for the past eight months. She stated that



her son and daughter have the same trouble and that she was nervous and easily upset. She presented combings of colored hair which she stated were from her own scalp, and asserted that she had not used dye. In consultation with the neuropsychiatric department, it was found that there was great conflict between her and her daughter. The onset of the illness was at the time of the death of the patient's husband and the disease is related to feelings of insecurity. The patient shows hypochondriac, hysterical and depressive trends. Serologic studies for syphilis were negative.

Examination shows the scalp to be normal in appearance. The hair is short and stiff, more so in some patches than others. There are several crusted excavations of the scalp but no evidence of green, red or blue hairs attached to the skin.

#### DISCUSSION

DR CARL LAYMON, Minneapolis. This patient was perfectly well until her husband died. Shortly after that, she said, her hair turned red, blue and green and it began to fall out. Improvement occurred until the war started and her son was inducted, after which the trouble recurred. The members of the staff at the university thought that she might be dyeing the hair that she plucked. Psychiatrists were consulted, and they made a diagnosis of psychoneurosis.

**Miliary Papular Tuberculid** Presented by DR FRANCIS LYNCH, St Paul

Mrs M O, aged 32, has an eruption which has been present on the nose for eighteen months, with occasional extension to the lips. Sulfathiazole ointment has not helped. Her general health is good. There is no history of exposure to tuberculosis. On the right ala nasi are about twenty red-brown small discrete papules, and there is one just above the margin of the upper lip. A diascopic examination showed the presence of a tuberculid. The Mantoux reaction (1:1000 dilution) was negative.

#### DISCUSSION

DR L H WINER, Minneapolis. A biopsy was performed and there were about six sections on the slide. I looked through two or three of them and did not find any tuberculous structure except a dilated follicle with hyperkeratosis in it. I reported it as a hyperkeratotic dilated follicle, then Dr Lynch called my attention to the last section of the slide, in which I noticed a single solitary giant cell, and it fitted the clinical picture of miliary sarcoid. I am rather skeptical a great deal of the time when I see a tuberculoid structure, but when the clinical picture bears out the microscopic findings I think that it can definitely be called tuberculoid.

DR FRANCIS LYNCH, St Paul. Miescher recently reported the results of microscopic study in about 50 cases of papular rosacea in which color and diascopic examination suggested the presence of a tuberculoid element. He found changes which he classified in three types: first, purely lymphocytic changes, second, those having a central epithelioid focus, and, third, those (the majority of specimens) showing tuberculoid structure, some resembling sarcoid and others lupus miliaris but without necrosis. He concluded that nodular rosacea and rosacea-like tuberculid are parts of the same disease, which is probably a benign tuberculid (*Dermatologica* 88:150 [Sept-Oct] 1943).

DR L H WINER, Minneapolis. What did he say the process was?

DR FRANCIS LYNCH, St Paul. He did not say.

**Dermatomyositis** Presented by DR JOHN MADDEN, St Paul

W W, a schoolboy aged 13, was admitted to the Ancker Hospital on Aug 17, 1944, because of inability to swallow. A week before this the patient noticed edema and erythema in the V of the neck and painful swelling of the arms and forearms. This was followed in two days by edema of the eyelids, larynx and

pharynx. The eyelids and V of the neck became heliotrope in color. The patient could not talk above a whisper, and even this required great effort. He was unable to swallow solid food and at the time of admission had difficulty in swallowing liquids. The legs became edematous, and the patient was unable to walk. He had mumps and acute mastoiditis accompanied with a subperiosteal abscess and subdural abscess in 1941. In April 1944, he had rheumatic fever and arthritis. The diagnosis of dermatomyositis was made on Sept 7, 1944. One hundred thousand units of penicillin was given daily. The penicillin was administered intravenously, subcutaneously and intramuscularly. It was found that the best response followed intravenous or subcutaneous administration. The edema of the eyelids and neck disappeared by September 16. There was a steady improvement in the speech and a decrease in edema of the larynx and pharynx. The patient became stronger and was able to sit up in a chair by September 23. The color of the skin had returned to normal by September 23. The edema of the arms and legs has decreased but is still present. The temperature has been normal most of the time but occasionally has risen to between 99 and 100 F. The patient was given 500 cc of blood plasma at intervals whenever the edema became great. This never failed to reduce the edema.

Laboratory examinations showed a hemoglobin content of 14 Gm and a white blood cell count of 3,200, the differential blood count showed polymorphonuclear neutrophils 54 per cent, lymphocytes 36 per cent, monocytes 4 per cent, plasma cells 1 per cent, eosinophils 1 per cent and immature cells 4 per cent. The urine was normal. The sedimentation rate of the blood was 10 mm per hour, the bleeding time one minute and thirty-five seconds and the coagulation time two minutes. The platelet count was 158,000.

#### DISCUSSION

DR JOHN MADDEN, St Paul. This boy has had remarkable results with penicillin. The symptoms reappear in about forty-eight hours when penicillin is stopped.

#### **Pityriasis Rosea (Tinea Versicolor?) with Leukoderma** Presented by DR JOHN MADDEN, St Paul

M N, a schoolboy aged 16, stated that he noticed a white spot on the chest in June 1944. About two weeks later the chest, shoulders and back were covered with similar but smaller lesions. The patient is dark skinned. The eruption consists of round or oval maculopapular, scaly, asymptomatic lesions varying in size from that of a bean to that of an olive.

#### DISCUSSION

DR S E SWEITZER, Minneapolis. I think that the skin should be scraped to see if fungi can be obtained from the scales. It has a typical fluorescence.

DR JOHN MADDEN, St Paul. This eruption did not fluoresce.

DR S E SWEITZER, Minneapolis. The lesions were not the right shape for pityriasis rosea.

#### **Multiple Superficial Epitheliomatosis** Presented by DR JOHN MADDEN, St Paul

A J H, an unemployed man aged 72, stated that lesions began to appear on his trunk about fifteen years ago. At present he has five superficial, pruritic, round or oval lesions from the size of a silver quarter to that of an egg scattered over the trunk. The lesions have a slightly raised, round, smooth, shiny border. The centers are crusted, excoriated, superficial ulcerations, some of which also show telangiectasia and scarring.

## DISCUSSION

DR S E SWITZER, Minneapolis I had a patient like this—only a good deal worse—a man of 24 or 26 years I treated four lesions recently with roentgen rays and cauterized about four more I think he had eight of them

DR JOHN MADDEN, St Paul This man has not been treated, and he complains of terrific itching at night

DR S E SWITZER, Minneapolis He is 72 years old probably he has a senile pruritus

**A Case for Diagnosis (von Recklinghausen's Disease?) Presented by DR JOHN MADDEN, St Paul**

The father of T P L, a boy aged 7, stated that a brown macule developed on the left side of the boy's chest just below the nipple in 1940 Since then many lesions have appeared, and the original lesion now covers the entire left half of the trunk Most of the lesions are deep chocolate brown asymptomatic macules There also are small macular lesions of leukoderma scattered over the cutaneous surface The patient has a soft, painless, egg-sized tumor over the lumbar portion of the spine He is thought to be mentally subnormal Roentgenograms showed only two carpal bones, which is the usual number in a child of 2 years

## DISCUSSION

DR FRANCIS LYNCH, St Paul Among the interesting clinical features were the small areas of depigmentation in ring form on the upper portion of the chest Is there a possibility that the boy has Albright's syndrome (hyperpigmentation skeletal abnormality, hyperthyroidism and disturbance of function of sex glands)?

**NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS**

**Harry C Saunders, M D, Chairman**

**Frank Vero, M D, Secretary**

**Nov 8, 1944**

**Generalized Sarcoidosis Presented by DR ISADORF ROSEN**

F L a woman aged 32 came to the clinic of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct 14, 1944 with a generalized eruption of seven months duration Scattered over the upper half of the back are numerous raised brownish red papules varying from 5 mm to 2 cm in diameter, of fairly firm consistency A few such lesions are present on the outer aspect of the left arm and on the face On the outer aspect of the arms numerous subcutaneous nodes are felt On the nose there is an elongated raised lesion of soft consistency, 1½ inches (3.8 cm) long, of light brownish-reddish color surrounded by a few tiny lesions The patient stated that she has lost 27 pounds (12.2 Kg) during the last year

The patient is married and has no children Her mother is said to have diabetes A brother has had asthma since childhood

General examination showed the inguinal and axillary lymph nodes to be enlarged On auscultation of the lungs it was found that the breath sounds were increased in intensity and on percussion there were some patches of dullness The liver was felt 3 fingerbreadths below the costal margin and was somewhat nodular The spleen was felt 2 fingerbreadths below the costal margin and was of hard consistency

The urine and blood counts were normal, and Wassermann and Kahn reactions of the blood were negative. Tuberculin tests elicited negative reactions with a dilution of 1:1,000. Roentgenograms of the chest showed generalized spotty and reticular peribronchial infiltration of both lungs, more pronounced on the right compatible with sarcoidosis. Roentgenograms of both hands revealed no changes in the bone.

Biopsy of lesions on the back and the nose was reported as indicating sarcoid.

#### DISCUSSION

**DR E. WILLIAM ABRAWOWITZ** This patient presents most of the features of sarcoidosis. The lesion on the nose was at first suspected of being lupus vulgaris. Attention is called to the invisible but palpable subcutaneous nodules on the arms which are of diagnostic significance. The patient's lungs are affected, and a biopsy of cutaneous lesions confirms the clinical diagnosis.

**DR MABEL G. SILVERBERG** I cannot recall that enlargement of the liver has been reported as due to sarcoidosis.

**DR E. WILLIAM ABRAWOWITZ** An enlarged spleen is not uncommon.

**DR FRED WISE** I should like to hear expressions of opinion as to therapy.

**DR ANTHONY C. CIPOLLARO** Most patients with sarcoidosis get well. The usual treatment is rest, well balanced diet, administration of an arsenical preparation and roentgen therapy. It is my understanding that sarcoids respond fairly satisfactorily to roentgen rays.

**DR GIRSCH D. ASTRACHAN** About a year ago I presented a case for diagnosis (*ARCH. DERMAT. & SYPH.* 50:223 [Sept.] 1940) before this section. Late secondary syphilis and sarcoidosis were suggested as possibilities. The final diagnosis of sarcoid was made a few months later. The patient did not respond to antisyphilitic treatment at first, but after she had received twenty-six additional injections of a bismuth preparation the cutaneous eruption showed a definite improvement.

**DR CHARLES WOLF** Recently I had an opportunity of seeing a patient with extensive sarcoidosis in the wards of Mount Sinai Hospital. The chief of medical services stated that sarcoidosis of such extensive nature, with involvement of various organs, is common in the South. One can always find 3 or 4 patients in the wards of the hospitals. As regards the outlook, it is discouraging to see the dissemination and the enormous number of lesions present, with involvement of organs. These patients as a rule eventually have acute miliary tuberculosis, either of the meningeal or of the pulmonary type. Various supportive treatments have a beneficial effect on the cutaneous lesions. For mediastinal or pulmonary involvement, roentgen ray therapy is efficacious in clearing up localized masses.

**DR ISADORE ROSEN** I was struck by the fact that every one of the lesions was unusually red, with a decided inflammatory areola, decidedly different from the type usually seen, which are either skin colored or brownish red. The lesions on the nose were raised and soft and clinically suggested either lupus vulgaris or lupus tumidus. I was greatly surprised that biopsy of one of the lesions from the nose was reported as showing sarcoid.

**Necrobiosis Lipoidica** Presented by **DR E. WILLIAM ABRAWOWITZ**

**L. S.**, a woman aged 44, came to the clinic of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on May 22, 1943, with an eruption on the legs of one year's duration. On the extensor surface of both legs are several large brownish plaques with raised, infiltrated borders and with telangiectasia in the center.

The past and family histories were noncontributory.

Results of urinalysis, blood count, determinations of blood sugar and sugar tolerance tests were normal. The blood cholesterol level was 255 mg. per hundred cubic centimeters. The Wassermann reaction of the blood was negative.

Biopsy was reported as showing necrobiosis lipoidica

The patient has received about eighty treatments with mecholyl by iontophoresis, with some improvement

#### DISCUSSION

DR FRED WISE This is a beautiful example of the eruption. It is especially interesting because of the negative history concerning diabetes and the lack of a diabetic family history.

DR EUGENE F TRAUB Attention should be called to the striking border on this lesion. This is the first time that I have seen a definitely elevated and almost rolled border such as might be seen in granuloma annulare. I presented several cases, both here and at the New York Dermatological Society, of this disease without diabetes, in which the diagnoses of granuloma annulare and morphea were considered, but in none of the cases was there an elevated border such as is seen in this case. Attention has previously been called to the differences of opinion as to the exact classification of some of the early cases, but I think that cases of necrobiosis lipoidica may occur without diabetes and should not be confused with granuloma annulare, morphea or any other process.

DR E WILLIAM ABRAMOWITZ Apparently a diagnosis of necrosis lipoidica without diabetes is accepted. The patient has a rather high blood cholesterol level. I had an opportunity to look at the slide this afternoon, and areas of infiltration could be seen in the cutis but no necrosis was present. There were giant cells and the development of fibroblasts, indicating replacement and involution. That may account for the unusual appearance of the lesions at present. The patient has been receiving mecholyl locally by iontophoresis with some benefit.

#### Granuloma Annulare with Lesions Limited to the Face and Resembling Basal Cell Epitheliomas Presented by DR EUGENE F TRAUB

B G, a Polish woman aged 51, came to the clinic of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital one week ago, complaining of lesions of the face. She stated that two months ago she noted a small lesion on the left side of the bridge of the nose. She thought that her eyeglasses had irritated the area and thought nothing of it, as there was no pain or itching. About one month ago she noticed similar lesions on the upper part of the right cheek, the right temporal region, the left temporal region and the forehead.

There is a history of allergy in the family but no personal history of allergy. The patient has been treated at the dermatologic clinic for two years for generalized pruritus and urticaria.

On the left side of the bridge of the nose there is an oval, slightly circinated, annular lesion about 1 cm in diameter. The center is depressed, with an elevated border consisting of small skin-colored nodules. The other lesions present the same aspect but differ slightly in size, and their centers are not so depressed. These lesions also have small nodules. There are no subjective symptoms.

A biopsy specimen of a lesion from the right temporal region was reported as suggestive of granuloma annulare, with no evidence of basal cell epithelioma.

#### DISCUSSION

DR FRED WISE I agree with the diagnosis as presented and am inclined to exclude other diagnoses.

#### Pityriasis Rubra Pilaris Presented by DR DAVID BLOOM

C F, a woman aged 30, came to the clinic of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in July 1944, with an eruption of four months duration. She presented on the back and chest a sharply defined erythema with a brownish tinge, with reddish-brownish papules near the borders of the plaques. The arms showed a similar eruption and the

face and scalp showed erythema and pronounced scaling. On the elbows and knees there were plaques suggesting psoriasis. The palms and soles were hyperkeratotic.

The patient improved considerably after ingestion of vitamin A, 75,000 units daily, for several months. She now presents erythema, lichenification and scaling on the back, particularly in the region of the sacrum and the superior portion of the intergluteal fold. The arms and chest are similarly affected. The scalp shows pronounced scaling, and there is a scaly plaque on each elbow and knee. The palms and, to a lesser extent, the soles show hyperkeratosis.

The past and family histories are essentially noncontributory.

A biopsy specimen showed changes compatible with pityriasis rubra pilaris.

#### **Pityriasis Rubra Pilaris** Presented by DR. DAVID BLOOM

S. L., a man aged 57, was previously presented at the Manhattan Dermatologic Society, in January 1944.

He now presents on the face, neck, flanks and abdomen fawn-colored diffuse well defined plaques, with clear skin anteriorly from the neck to above the umbilicus and posteriorly from the neck down to the lumbar region. Similar plaques involve the lower portion of the buttocks and the posterior aspect of the thighs and also the pubic region. On the buttocks and elbows there are scaly plaques suggesting psoriasis. The scalp shows pronounced scaling. The patient is mentally confused.

Blood counts on several occasions showed fairly normal values. The Wassermann reaction of the blood was negative. The urine was normal. The biopsy report was superficial dermatitis.

Treatment has consisted of injections of liver extract, and vitamin A and bromides by mouth.

#### DISCUSSION OF CASES OF PITYRIASIS RUBRA PILARIS

DR. ISADORE ROSEN: I do not want to disagree with the diagnosis, but I have seen similar manifestations in patients who have had extensive involvement in psoriasis.

DR. FRED WISE: Both the man and the woman patient have, in my opinion, eruptions of pityriasis rubra pilaris. In the case of the man, it is of interest to note that there is at present an absence of follicular hyperkeratosis of the dorsal surfaces of the fingers.

DR. E. WILLIAM ABRAMOWITZ: When the man first appeared in the clinic, I thought that he had pityriasis rubra pilaris. He had follicular lesions on the back of the fingers, but he had been applying a good deal of oil and an oil folliculitis was a possibility. Biopsy at that time showed only a superficial type of dermatitis. The patient has had this eruption on his body for about two years. I am inclined to accept the diagnosis as presented.

In the case of the woman, the scaly lesions on the elbow, the characteristic pitting of the nails and the scaly patches with sharply circumscribed borders on the buttocks as they appear tonight are more in favor of psoriasis. The appearance of the eruption at the onset was more like pityriasis rubra pilaris.

DR. EUGENE F. TRAUB: I understand that Dr. Bloom had microscopic confirmation of his diagnosis in one case. In this respect I think that he is fortunate, for I had a typical example of this disease in which every one concurred clinically, but four biopsies were performed before anything at all typical or suggestive of the process was forthcoming. I have had this experience before, in other instances of this dermatosis, hence I believe that histologic confirmation may sometimes be difficult.

DR. DAVID BLOOM: The reason for the presentation of these 2 cases is the fact that pityriasis rubra pilaris is typical only in the beginning. Later, when the follicular spinulose papules have coalesced to form plaques, the roughness may disappear entirely and the case is not recognized as one of pityriasis rubra.

pilaris In the man presented tonight, even the microscope did not reveal follicular hyperkeratosis When he was first observed, there were typical follicular papules on the back of his hands and fingers, which later disappeared, but tonight some of them have reappeared

In the case of the woman, the picture was typical in the beginning of pityriasis rubra pilaris, and the diagnosis was confirmed by histologic examination Tonight, not every one is willing to agree with this diagnosis I am reluctant to disagree with Dr Rosen, from whom I originally learned dermatology, but I cannot help being impressed with the fact that the appearance of the cutaneous changes in both patients is strikingly different from that of psoriasis

In the man mental confusion developed, for which he was referred to the mental hygiene department There the opinion was expressed that the changes in the brain are possibly due to the same toxins which have caused the changes in the skin

### MANHATTAN DERMATOLOGIC SOCIETY

George M Lewis, M D, *Chairman*

Wilbert Sachs, M D, *Secretary*

Nov 14, 1944

#### Tuberculosis Orificialis Presented by DR MAURICE J COSTELLO

E H, a married woman aged 38, from St Joseph's Hospital for Consumptives, had a sore on the floor of her mouth about three years ago She had a cough at that time A physician at the New York University Clinic performed a biopsy of the lesion, which showed a tuberculous structure A roentgenogram of the chest showed pulmonary tuberculosis, which is now controlled by pneumothorax on the left side

The oral lesion is nickel sized, oval and crateriform with a rounded, elevated border The center of the lesion is ulcerated and is covered with a grayish exudate There is some limitation of motion of the tongue due to adhesion to the floor of the mouth There is tenderness and moderate pain when hot or spicy foods are eaten

There is also a scar on the left side of the neck which the patient claims was active at the time of the appearance of the lesion in the mouth

The sputum contains no tubercle bacilli, but a smear from the ulcer showed acid-fast bacilli

#### DISCUSSION

DR DAVID BLOOM I agree with the diagnosis Apparently the patient has tubercle bacilli in the lesion Are these bacilli furnished by a focus in the lungs, or have they persisted in the ulcer since its formation?

DR FRED WISE Most textbooks mention the use of a lactic acid solution as an effective remedy

DR HERMAN SHARIT Dr Costello asked me privately whether ozonides would be of any use in this case They have been reported by several genitourinary specialists as being valuable in the treatment of tuberculous sinuses Ozonides are continuously releasing nascent oxygen, and this may be helpful in tuberculous sinuses and might be helpful in this case

DR E WILLIAM ABRAWOWITZ In the Pfannenstiel treatment, wicks of strong hydrogen peroxide were placed in the ulcerated area and sodium iodide was given orally This caused the liberation of iodine at the site of application, followed by healing of the ulceration These ulcerations usually appear in the late stages of active tuberculosis of the respiratory apparatus Is this possibly an inoculation tuberculosis ulcer in a patient with healed tuberculosis of the lung?

DR ISADORE ROSEN To me, the unusual feature of the case is that the diagnosis of tuberculosis was made from the ulceration of the mouth rather than from the pulmonary symptoms. It seems to me that for a woman to have such active lesions of the lungs as shown by the roentgenograms she must have had symptoms suggesting pulmonary tuberculosis prior to the development of the lesion in the mouth.

DR ANTHONY C CIPOLLARO I am interested in this case because tuberculous ulcerations of the mouth are rare. They occur as a result of a direct extension from an active pulmonary tuberculous process. Tuberculous ulcerations in the mouth are indicative of such lowered immunity that a fatal outcome is imminent. The patient presented this evening has an ulcer of the mouth, diagnosed as tuberculous, which has been present for three years. During this time the pulmonary condition has improved, the ulcer has persisted, and the patient does not appear to be moribund. This is most unusual. Dr Costello states that a recent smear taken from the ulcer showed tubercle bacilli and a biopsy showed tuberculous structure. Dr George Wilson has treated many patients with laryngeal tuberculosis at Saranac Lake with electrocoagulation. I wonder whether that would not be a good procedure in this case. I wonder also whether this might not be a suitable case for treatment with ultraviolet radiation from a water-cooled quartz mercury vapor arc lamp.

DR GEORGE C ANDREWS This impressed me as a straightforward case of tuberculous ulcer of the mouth. I have treated many patients with benefit, and I think that the safest method is either with ultraviolet irradiation or with radium. A radium plaque placed in the floor of the mouth, as in the treatment of angioma, will probably heal this ulcer. I think that tuberculin is dangerous to use in a case like this. The patient still has extensive tuberculosis in her lungs. One must be cautious as to prognosis.

DR FRED WISE I do not understand exactly what Dr Cipollaro intends to imply, and I should like to ask him this question: Does arrested pulmonary tuberculosis exclude the existence of an active oral tuberculous infection?

DR ANTHONY C CIPOLLARO The usual conception of the development of orificial tuberculosis is this: First there is active pulmonary tuberculosis. Then an ulcer appears in the mouth, which is a direct extension of the tuberculous process in the lungs to the mouth through the expectoration. These ulcers develop because the patient is no longer able to form antibodies to destroy the tubercle bacilli. The tuberculin tests show a negative energy. Because the patient has no resistance whatsoever, a fatal outcome is usually imminent. One does not expect a patient with tuberculous ulcers of the mouth to live for three years. If this is a tuberculous ulcer, physicians must change their conception of what has been taught them about the nature of the disease and its prognosis in patients in whose mouths ulcerations develop.

DR GEORGE M LEWIS Provided there is no active focus in the lungs, are tuberculous ulcers in the mouth responsive to treatment?

DR ANTHONY C CIPOLLARO Dr MacKee advocates the use of roentgen rays in treating orificial tuberculosis. Apropos of Dr Andrews' remarks in recommending the use of radium, he and Dr MacKee agree that irradiation is a painless and effectual method of treating orificial tuberculosis.

DR MAURICE J COSTELLO I have had no experience with the treatment of tuberculous ulcers of the mouth with lactic acid, although it is mentioned as an effective treatment of these lesions. This patient had a cough for a long time, but it never made her suspect pulmonary tuberculosis. Soon after an ulcer had developed on the floor of the mouth, she visited the New York University Clinic. A tuberculous ulcer was suspected, biopsy confirmed the diagnosis, and she was referred to the thoracic service of the Bellevue Hospital, where roentgenographic examination of the lungs disclosed diffuse advanced tuberculosis. The difficult thing to understand in this case is that the pulmonary tuberculosis has improved



so much while the tuberculous lesion in the mouth has remained stationary I think that it can be explained by the fact that even though her sputum contains no tubercle bacilli the patient has advanced pulmonary tuberculosis with a large quantity of sputum and she may occasionally have tubercle bacilli in the sputum which would prevent the ulcer from healing I think that what Dr Cipollaro says is usually true that when a person contracts tuberculosis orificialis the prognosis is grave and a fatal outcome may be expected The patient has received roentgenotherapy in a dosage of 100 r, unfiltered, at weekly intervals, with some improvement

#### Keratosis of Palms (Treated) Presented by DR GEORGE M LEWIS

E D, a man aged 37, has had psoriasis affecting various parts of his body for the past six or seven years Lesions developed on his hands over a year ago and have persisted When he was first examined, on Aug 23, 1944, there were punctate, keratotic lesions scattered over the palms and fingers Typical psoriatic lesions were noted on the elbows and on other parts of the body The patient has been treated by means of local application with an ozonide compound, as well as with other keratolytic agents The response has been more gratifying than one usually expects in cases of this type

#### DISCUSSION

DR HERMAN SHARLIT I presented before this Society 2 patients with keratosis of the palms which cleared up with the use of ozonides of olive oil Neither of these presentations found its way into print Ozonides are compounds of oxygen with unsaturated fatty acids, the oxygen being bound as  $O_2$  These compounds are produced by driving a source of oxygen through the fatty acid mixture in the presence of a metal catalyst In the case of the product I am using, the source of the fatty acid is olive oil The ozonide is never removed from the oil which simply remains as a vehicle for the ozonide This particular ozonide mixture contains approximately 25 per cent ozonide in olive oil Ozonides are able to penetrate into the skin, which differentiates them from the inorganic peroxides, which have no such penetrating powers This mixture of ozonide in olive oil is continuously giving off nascent oxygen This can readily be demonstrated in the following manner Mix potassium iodide crystals with starch, make a water paste and add a few drops of the ozonide mixture A blue color immediately begins to form in the mixture, indicating that iodine has broken off from the iodide and has reacted with the starch to give the blue color

DR THOMAS N GRAHAM It is certainly an excellent result

DR ISADORE ROSEN I should like to know whether the keratotic lesions were due to psoriasis or to arsenic Has a definite diagnosis been established?

DR JACK WOLF I was about to raise the same question as Dr Rosen did Lichen planus, psoriasis and some other dermatoses cause hyperkeratotic eruptions on the palms, and I am wondering whether the patient did not present the cribriform eruption of the palms occasionally encountered in psoriasis This man has no other keratoses on the dorsal aspects of the fingers, where one would expect to find them as a result of taking arsenic I think that a positive diagnosis must be established before the response to therapy can be gaged

DR GEORGE M LEWIS Although there is no history of ingestion of arsenic, the lesions were typical of arsenical keratoses There has been such a satisfactory response that little evidence of the disease remains As is generally known, treatment in similar cases has heretofore been unsatisfactory I believe that Dr Sharlit's treatment is worthy of further trial

#### Psoriasis? Roentgen Ray Dermatitis of Groins, Scrotum and Scalp, Roentgen Ray Ulcer of Perineal Area Presented by DR E WILLIAM ABRAMOWITZ

M R, a man aged 59, a private patient, is a Russian Jew, now residing in Canada About twenty years ago an eruption developed in the groins and perianal

area, accompanied with severe itching. For twelve years, up to two years ago, he received four or five roentgen ray treatments yearly to these areas from a roentgenologist. He also received a smaller number of treatments to a scaly patch on the left parietal area of the scalp.

The groins now present numerous telangiectases extending to the under surface of the scrotum and involving the perianal area and buttocks. At the upper pole of the median raphe there is an erosion 1 inch (2.5 cm) by 1½ inches (3.8 cm) in size. This lesion developed in August 1944, when it was twice as large as it is at present. It has receded under bland topical applications. The patient also presents scaly papules with some suggestion of telangiectasia and atrophy in the left parietal area of the scalp and leukoplakia of the mouth. He complains of itching and pain in the perineal area. No palpable lymph nodes are present. The general physical condition is good.

The patient is presented for suggestions as to therapy of the ulcerative area in the perineal region.

#### DISCUSSION

DR HERMAN SHARLIT. Obviously the patient has had a radiodermatitis. There is no accounting for the background, which may have been psoriasis.

DR MAX SCHEER. The ulcers may heal, but they will break down again, and I think that ultimately surgical excision will have to be resorted to. Dr Abramowitz pointed out some telangiectases on the patient's scalp, in which area, he said he had received some roentgen ray therapy. However, I doubt that this could have been the cause, since I could see no alopecia in those areas.

DR JACK WOLF. Temporarily, I think that this man might receive a period of conservative therapy in an attempt to heal the ulcer. Rest in bed and a bland cream kept on at all times to avoid friction may lead to healing. If the area should break down again, I see nothing else except surgical removal and plastic repair.

DR MIHRAN B. PAROUNAGIAN. I think that Alvagel (an ointment prepared from Aloe vera) is an excellent remedy for this type of radiodermatitis.

DR DAVID BLOOM. The presentation of this case is fully justified, for it again calls attention to the fact that most cases of radiodermatitis produced by the treatment of cutaneous diseases have been caused by excessive treatment given by general radiologists. Being accustomed to administer large doses of roentgen rays for malignant growths and having insufficient knowledge of dermatology, the general radiologist overexposes the skin to the rays and underestimates the importance of sequelae such as telangiectases. Unless a radiologist has had special training in dermatology and in the treatment of cutaneous diseases, he should treat dermatologic conditions only in collaboration with the dermatologist.

DR MAURICE J. COSTELLO. I think that the reason an ulcer developed on the perineum and not on other areas is that there might have been some overlapping of roentgen rays when the patient was exposed from the front and then from the back.

DR GEORGE M. LEWIS. I should like to ask Dr Abramowitz whether he has thought of using Aloe vera. I have had good results in several cases.

DR MAX SCHEER. In private practice I have followed up a number of patients with ulcerations from roentgen ray and radium therapy. Even if the ulcers heal for a time with Aloe vera or other remedies, the healing is not permanent. They have always broken down again. The patient can be saved possibly months or years of suffering if surgical excision is performed at the start. I have never found any other method which was of more than temporary benefit.

DR GEORGE M. LEWIS. To answer Dr Scheer, I might remind him that I presented before this Society last year a patient who had radiodermatitis with ulceration treated with Aloe vera. The lesion is still completely healed. It has now been well for over two years, and the skin is firm, with no sign of breakdown.

DR GEORGE C ANDREWS I can vouch for the fact that the skin looks healthy

DR ANTHONY C CIPOLLARO I have had similar good results with the use of Aloe vera

DR E WILLIAM ABRAMOWITZ I am not certain that this man has psoriasis. He has some scaly patches suggesting psoriasis, and it is possible that the original lesions in the perianal area were also psoriasis. The patient has a radiodermatitis with an ulceration in the perineal area. What is the best therapy to use? One always fears the ultimate development of malignant changes. In this instance, the ulcer receded to almost one-half its size with the use of zinc oxide ointment containing some essential oils. I think therefore that it might not be amiss to use something conservative such as an ointment containing cod liver oil or Aloe vera. If the ulcer healed and then recurred, it would probably require excision and plastic repair. The Aloe vera leaf is difficult to obtain but the ointment can still be had.

### **Pityriasis Rosea Resembling Secondary Syphilis** Presented by DR ISADORE ROSEN

R W, a woman aged 29, registered at the clinic of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Nov 12, 1944, complaining of a generalized eruption of ten days' duration. The eruption involves the anterior aspect of the trunk from the breasts down to the pubis, flanks, lower part of the back and buttocks. It consists of erythematous raised papules, mostly of oval shape, with some showing a scaly collaret. In the left groin there is a larger lesion which preceded the generalized eruption by about two days. There is only slight itching. The Wassermann reaction of the blood has not yet been reported.

#### DISCUSSION

DR WILBERT SACHS I think that the unusual feature is the fact that the confusion between pityriasis rosea and secondary syphilis does not occur oftener. The histologic changes in the two may be similar in the early stages. The patient admitted to Dr Wise that there is itching, and there was a herald patch, hence, I am more inclined to believe that the disease is pityriasis rosea than that it is secondary syphilis.

DR GIRSCH D ASTRACHAN I agree with Dr Rosen that this eruption suggests the possibility of syphilis. However, there are several features which speak against this diagnosis. First, the color is bright, while in syphilis it is dull. Second, the eruption is localized to the abdomen and back, while in syphilis it would be generalized. The absence of lesions on the palms, soles and mucous membranes, together with the absence of polymorphism of lesions, speaks against the diagnosis of syphilis.

DR MIHRAN B PAROUNAGIAN I think that it is a good thing that Dr Rosen presented this case, because a mistake might be made in the hands of inexperienced dermatologists. I have seen many similar cases of pityriasis rosea diagnosed as syphilis.

DR GEORGE C ANDREWS I agree.

DR MAURICE J COSTELLO I have often heard Dr Fox say that the only importance of pityriasis rosea is to differentiate it from secondary syphilis.

DR HERMAN SHARLIT I am inclined to feel that there is no such thing as an absolute clinical differentiation between syphilis and pityriasis rosea when the pityriasis rosea does look like syphilis except by proving with serologic tests that it is not syphilis.

DR THOMAS N GRAHAM In addition to the features mentioned by Dr Astrachan, I think that all the lesions are definitely oval, and I do not recall any case of secondary syphilis in which this was true. The lesions in syphilis are more inclined to be round. Also, the lesions in this case definitely follow the lines of cleavage, a distribution which is not observed in syphilis.

DR ISADORE ROSEN This case struck me as unusual. The uniformity of the lesions and the absence of the superficial scales usually seen in pityriasis rosea gave this eruption the appearance of a maculopapular syphilid. The only feature against this diagnosis was the color. I have never seen such a close resemblance to secondary syphilis as in this instance.

**Blastomycosis** Presented by DR ANTHONY C CIPOLARO

J M, a man aged 52, born in England, first attended the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on May 8, 1944, complaining of a lesion on the right side of the neck of one year's duration. The lesion discharged a purulent material and had been gradually growing. The use of various topical applications had had no influence on the lesion.

On examination at that time there was a round lesion, approximately 3 inches (7.6 cm) in diameter, on the right side of the neck. The periphery was elevated and erythematous. The center was bright red, exudative and sieve-like. Slight pressure on the surface of the lesion caused a purulent discharge to exude from the many tiny openings in the center.

Several mycologic examinations, including cultures, failed to reveal the blastomycetes. On biopsy the disease was reported as possible blastomycosis. The Wassermann reaction of the blood was negative, and the urine and the blood count were normal. A specimen of blood was sent to Dr David T Smith, of Duke University, for an agglutination test, but it was hemolyzed on arrival and unfit for testing.

In the belief that the lesion was one of blastomycosis, it was treated intensively with roentgen irradiation. Between March 26 and June 12, 1944, he received  $2\frac{1}{2}$  units (1,375 r) of filtered (3 mm of aluminum) roentgen rays in fractional and semi-intensive doses. The lesion healed with this treatment, except for a portion along the lower edge. This was closely shielded, and additional radiation was applied in semi-intensive doses at intervals of every few days. Between June 26 and September 29, he received to this area an additional six erythema doses (3,300 r) of roentgen rays. The lesion had not responded completely, and it was decided to give him intravenous injections of sodium iodide. After the second injection this medication had to be suspended because of a severe gastrointestinal upset, with vomiting, diarrhea, etc.

DISCUSSION

DR WILBERT SACHS I saw this patient some months ago, and he then had all the features that one would expect to find in blastomycosis. I think that the response to treatment has been excellent. Microscopic examination showed blastomycosis, but I could not find the organisms and therefore hesitated to make that diagnosis, knowing that several other diseases may give a similar histologic picture.

DR GIRSCH D ASTRACHAN I was much interested in Dr Cipollaro's account of the reaction following the administration of sodium iodide. I have always felt that even with sodium iodide one should be careful and increase the dose gradually. I had an experience with a patient for whom I prescribed potassium iodide orally. After one or two doses of 5 drops each the patient returned to my office the same day with his tongue so swollen that he could not speak—a real macroglossia. The swelling decreased and the tongue became normal in a few hours.

DR MIHRAN B PAROUNAGIAN I agree clinically with the diagnosis of blastomycosis.

DR GEORGE C ANDREWS I think that the result of treatment is excellent. I recently treated a patient with blastomycosis, he had already received roentgen

ray therapy with resultant atrophy and consequently could not be given more. He had verrucous inflammatory lesions on the forehead and face and was treated with iodides. The reason I mention this case is that the patient became depressed from potassium iodide in large doses. I had a similar experience with another patient, who was later able to tolerate 1,000 grains (64.9 Gm.) a day by mixing equal parts of ammonium, sodium and potassium iodides.

DR FRED WISE. If I recall correctly, a blastomycin skin test was described at the International Dermatologic Congress held in Budapest, Hungary, in 1935.

DR GEORGE M. LEWIS. I agree with Dr. Rosen that laboratory confirmation is important and should precede active therapy. It is my opinion that iodides and roentgen rays are not particularly effective for blastomycosis. In cases of early infections, certainly, the best treatment is complete surgical removal by excision or by curetting away the entire mass and following with electrodesiccation. Even fairly large lesions are still amenable to that treatment.

DR GEORGE C. ANDREWS. These lesions are frequently too far advanced to permit surgical excision, and there has been some feeling that excision might cause the disease to spread internally. Sulfonamide drugs were mentioned. I gave my patient a full course of sulfadiazine without improvement, and also 2,000,000 units of penicillin without benefit. Iodides and roentgen therapy seem to give the best results.

DR ANTHONY C. CIPOLLARO. I am sorry that the diagnosis was not better established, but before the patient came to me several eminent clinicians made a clinical diagnosis of blastomycosis. Careful mycologic and pathologic studies were made, but the results, although suggestive, were not conclusive. From my own clinical observation the lesion was typical blastomycosis, and, as Dr. Sachs has just admitted, the histologic picture is that of blastomycosis, but he refused to make the diagnosis because he could not find the organism. There is no question that the disease responded well to heavy doses of roentgen rays, and there is no question that the patient will have some changes in his skin due to irradiation, but the disease is a serious one which could end fatally. I had a similar case in which the patient was cured with roentgen ray therapy, but pulmonary lesions developed and some two years later the patient died. I cannot help feeling from my limited experience and short observation that it is extremely difficult to demonstrate and culture blastomycetes in cases such as the one presented tonight.

#### Generalized Progressive Scleroderma Presented by DR ANTHONY C. CIPOLLARO

F. A., a 42 year old man, a machine operator, born in Italy, consulted me on Aug. 25, 1944 because of an eruption of eighteen years' duration. He is married and has five children who are living and well. No members of the family have died. The patient states that he had rheumatoid arthritis twenty years ago which necessitated hospitalization for six months, since then he has had no recurrence. About eighteen years ago he first noticed that his skin became hard and white. The whiteness would be most pronounced in the winter months. The tips of the fingers would become sore after the slightest injury or even a scratch mark, and months would elapse before these sores would heal. Recently he has had no lesions on his finger tips, but ulcers have developed on various portions of his legs, and these have been extremely painful and persistent. The smaller ones would heal in a matter of months, and the larger ones would persist for years. He also suffers from intense pain affecting the feet and the legs. The pain is especially severe when he tries to walk in his bare feet. It also interferes with his sleep. He has been hospitalized and under the care of physicians on and off during all these years. Numerous laboratory examinations have been performed all of which revealed normal conditions.

The skin of the face is hard and moderately hidebound, does not wrinkle easily and has a peculiar pallor. There is a pinched expression. The hands are hard and partially stiff. The skin of the fingers is thick and white and lacks elasticity. The fingers taper down to a fine point. There are some scars of old ulcers on the tips of some of the fingers, and the subungual regions show some hyperkeratosis. In cold weather the hands are white. There are a number of ulcerated areas on the outer side of each leg. On the right leg the ulcer is large, irregular, about 0.5 cm deep, punched out and dry. There are thirty or more scars of different sizes and shapes scattered over both legs. The toes show changes similar to those of the fingers, but to a much lesser degree. Scattered over the hands, arms, face and neck are telangiectatic vessels and small lesions resembling spider nevi, which the patient states he has had practically all his life.

The patient has been receiving weekly intravenous injections of 100 mg of sodium nitrite and has been using sulfathiazole powder on the ulcerated areas. Many of the ulcers have improved and the active ones have dried up. About three weeks ago he was given erythryl tetranitrate in  $\frac{1}{4}$  grain (0.015 Gm) doses, in addition to the intravenous injections of sodium nitrite. For the pain he has been taking acetylsalicylic acid with codeine. The patient has shown steady improvement with this treatment. His general health has improved, and the local condition is better.

#### DISCUSSION

DR MAURICE J. COSTELLO: I think that this patient has gone through all the changes, including dermatomyositis and scleroderma, and, in addition, has rectangular areas of telangiectasia on the face and buccal mucous membranes which have impressed me greatly as a constant feature of calcinosis cutis, scleroderma, dermatomyositis and other diseases.

DR E. WILLIAM ABRAMOWITZ: I think that the patient has sclerodactyly and there are numerous telangiectases on the face and the trunk and also in the mouth. These may be two separate and unrelated dermatoses. The ulcers on the legs would not be unusual in scleroderma. Vegetating verrucous lesions around the ulcer may occur after long-continued use of ointments, especially petrolatum. I should investigate the family history for hereditary telangiectasia. Dermatomyositis associated with Raynaud's syndrome is also a possibility.

DR JACK WOLF: I agree with the remarks of Dr Costello, especially with regard to rectangular telangiectasis, since it occurs in a certain type of severe scleroderma.

DR ANTHONY C. CIPOLLARO: I presented this case because Dr Costello has shown several similar ones. When I referred to the literature on scleroderma, Raynaud's syndrome and dermatomyositis, I found it difficult to incorporate all the symptoms that this patient presents under any one of these categories. This is an extremely confused clinical picture, and the name "scleroderma" does not cover the lesions which this man presents. The telangiectases which Dr Costello mentioned appeared many years ago, about the same time as the disease. The patient gives a history of having had a severe infection accompanied with arthritic symptoms, which required hospitalization for six months. This is seen in cases of dermatomyositis. I really should have presented the case as one of scleroderma with a question mark. The skin definitely does not wrinkle. The patient now presents one large ulcer, but two months ago he had half a dozen ulcers on each leg. I should like to attribute the improvement to the local use of sulfathiazole powder and to the administration of vasodilators. I decided on sodium nitrite, for it produces prolonged vasodilation. Dr Walter Duggan of Utica, N. Y., has cured many patients with tobacco blindness and other diseases of the eye with this drug, and he was the first to bring to my attention its value in scleroderma and other cutaneous diseases.

## LOS ANGELES DERMATOLOGICAL SOCIETY

A Fletcher Hall, M D , *President*Clement E Counter, M D , *Secretary*

Nov 14, 1944

**A Case for Diagnosis (Syphilitic Verruciform Melanoleukoderma?)** Presented by DR MOLLEURUS COUPERUS

A S, a woman aged 46 years, was born in the state of Jalisco, Mexico. She came to the United States at the age of 16. When she was 7, she had a "sore" on the back of the right leg, which remained for several months and left a brown pigmented area. The next year she had a generalized eruption which resembled chickenpox or smallpox. The present lesions are said to have appeared first on the feet two years ago. This eruption soon spread to the rest of the body. Some lesions were moist. Itching of some of the lesions was present at times.



Fig 1—Atrophic and hyperpigmented lesions on the chest

She was married the first time twenty-one years ago and the second time ten years ago. There have been seven pregnancies. The first four resulted in children who are alive and well. The youngest is 6 years old. The last three pregnancies resulted in miscarriages. The first of these was four years ago. Her present husband acquired syphilis at an early age. A Wassermann reaction of the patient's blood ten years ago was negative.

There is a crusted weeping eruption on the scalp and erythema, fissuring and crusting of the skin surrounding the ears and involving the pinna, suggesting a seborrheic dermatitis. There is a similar eruption in each inguinal region. There are also moderate fissuring and scaling between all toes. On the upper part of the chest, the back, the shoulders and the legs the patient has large oval lesions. Many of these lesions are about 1 cm wide and 4 cm long. Some are discrete and many are confluent, giving a serpiginous arrangement. Lesions are slightly elevated at the periphery, with slight, fine scaling margins. Many lesions are brownish red with pinkish white centers. A few areas have only the achromic area remaining. On both legs, lesions are hyperkeratotic. Several lesions in this area are dark brown and appear angiomatous in their centers. There are varicose veins of both legs.

The Wassermann reaction of the blood was first recorded positive two years ago. Tests of the spinal fluid gave normal results except for a moderate midzone rise on the colloidal gold test. The youngest child had a negative Wassermann reaction of the blood one year ago. The most recent Wassermann reaction of the patient's blood was negative.

The biopsies from three different lesions showed essentially the same conditions. There were hyperkeratosis and parakeratosis and considerable irregular acanthosis. There was a dilatation of the capillaries immediately beneath the epidermis, with a moderate amount of lymphocytic infiltrate. At the extremity of an enormously enlarged rete peg, there is a dense infiltrate of lymphocytes and plasma cells.



Fig 2—Hypertrophic lesions on the legs

There is also a perivascular infiltration of lymphocytes and plasma cells and an occasional epithelioid cell.

There has been continual antisypilitic treatment for the past eighteen months. This treatment has been alternate courses of bismuth subsalicylate and oxophenarsine hydrochloride.

#### DISCUSSION

DR HAL E. FREEMAN: I cannot consider this a syphilitic leukoderma. This was a syphilitic eruption, I believe, and there is depigmentation following an acute syphilitic process. Of course, in such a person one would think of leprosy, but the histologic section does not bear that out and the nasal smears do not show Hansen's bacilli. This is syphilis, but I do not believe that it is leukoderma syphiliticum.



DR H C L LINDSAY I agree with Dr Couperus that it is syphilis, notwithstanding its resemblance to lichen planus

DR KENNETH STOUT I feel dubious that the lesions are on a syphilitic basis I raise the question whether this might be a case of pinta The patient has lived in areas where pinta is common

DR SAMUEL AYRES This case shows an unusual picture I do not think that the possibility of syphilis has been disproved, because there is much in favor of it The lesions on the chest and back with pigmentary changes are unusual The verrucous and hyperkeratotic nature is unusual There seems to be a follicular hyperkeratosis over the trunk, which might point to a vitamin A deficiency There is a strong possibility that one is dealing with tertiary syphilis modified somewhat

DR M E OBERMAYER Pinta can be ruled out by the presence of extensive scarring The late stage of pinta is characterized by pigmentary disturbances, and only in some instances have lesions of long standing been known to become atrophic I should consider the possibilities of late syphilis, yaws and perhaps leprosy The atrophic scarring with peripheral hyperpigmentation, which was evident in every lesion, is suggestive of syphilis May I point out that in this patient a terminal phase of the cutaneous manifestations is being dealt with and not active inflammatory lesions? The presence of hyperkeratotic surface changes makes no difference in this respect, as such changes are not infrequently encountered associated with scarring of all types They represent an individual reaction of the patient rather than a specific manifestation of the disease

DR W H GOECKERMAN Why not consider one of the tropical diseases, such as leishmaniasis, since the patient is a Mexican? All that is to be seen today is atrophic scars of discrete, rounded type and of various sizes I do not believe that the scarring is the result of syphilis, because only healed discrete gummas could show such an appearance, and the history will not allow one to assume that such gummas were ever present

DR NELSON PAUL ANDERSON Does it not appear that this patient had had enough treatment to rule out the probability that these lesions are due to syphilis? I thought that the one histologic section was more suggestive of lichen planus than any other condition If Krajan's method was used in staining one section for organisms, I believe that the absence of spirochetes would exclude pinta Only a syphilis strongly resistant to treatment could possibly give this picture In such a case the Wassermann reaction of the blood should be positive

DR MOLLEURUS COUPERUS When the patient was first seen, lichen planus, pinta and late secondary syphilis were considered The biopsy did not seem to support the diagnosis of lichen planus A Krajan stain for spirochetes was negative Photographs sent to Dr F. Latapi in Mexico, D F, Mexico, were returned with the comment that he had never seen any pinta of that type He did not know what the eruption might be I do not know what the lesions are I felt that both the biopsy and the over-all picture were most compatible with an unusual late secondary or tertiary syphilitic lesion The Wassermann reaction has become negative The lesions have improved only slightly during the antisymphilitic therapy

#### Syphilis with Amyotrophic Lateral Sclerosis Presented by DR HAL E FREEMAN

A V J, a man aged 39 years, had a penile ulcer twelve years ago This was followed by a positive Wassermann reaction of the blood There has been a muscular "wasting" of the thenar and hypothenar areas during the past six years His father had a right hemiplegia, said to have been caused by acute poliomyelitis

The skin is normal The patient has red hair and an extensive distribution of lentigines The superficial tendon reflexes are bilaterally hyperactive The pupillary reflexes to light and in accommodation are normal Ankle clonus is present

The reaction to the Wassermann test of the blood was strongly positive six months ago. A test of the spinal fluid at the same time showed a weak positive reaction to the Wassermann test, a trace of globulin, a normal cell count and a normal colloidal gold curve.

Treatment for syphilis has consisted of five intramuscular injections of mercury and thirty intravenous injections of arsphenamine twelve years ago. There have been twenty-seven intravenous injections of tryparsamide in the past six months.

#### DISCUSSION

DR ALEX CAMPBELL (by invitation) I noticed that the patient was being treated with tryparsamide. If his amyotrophic lateral sclerosis is due to syphilis, I should think that it would be more correctly classified as a vascular neurosyphilis and that treatment should be with bismuth and a trivalent arsenical.

DR J WAITER WILSON This may be peripheral neuritis due to lead. The man has a history of being a painter for fifteen years.

DR HAL E FREEMAN I think that perhaps Dr Campbell is right and that tryparsamide is not indicated here. I have been giving the patient tryparsamide, on the theory that he had syphilis of the central nervous system. It has recently occurred to me that the amyotrophy might not be due to syphilis. I do not agree with the theory that this is a neuritis. The man has a positive serologic reaction. He does not have tabes. His reflexes are present and hyperactive, which is consistent with a diagnosis of amyotrophic lateral sclerosis, the cause of which could be syphilis.

#### Lentigo Presented by DR M E OBERMAYER

W H, a boy aged 10 years, was hit on his nose by a wooden bat two years ago. No visible injury of the skin was produced. Three days after the injury a black spot appeared on the nose, which remained unchanged. It has not grown and has caused no subjective symptoms. There is a black macule, about 1 cm in diameter, of irregular contour on the bridge of his nose. Diastopic pressure produces no change in color.

#### DISCUSSION

DR H C L LINDSAY The lesion is a dark brown mark made by some extraneous color introduced under the skin. It could be taken out easily with a minor operation without disfiguring or scarring.

DR W H GOECKERMAN I saw this patient and referred him to Dr Obermayer for his opinion on the therapeutic procedure. There was enough pigment to suggest a melanoma, but it is likely that some foreign substance may explain the pigmentation, since there is a history of trauma. I did not want to take a small biopsy specimen, and ordinary excision of the lesion might leave considerable deformity. A plastic surgeon could probably handle it best.

DR SAMUEL AYRES This case is a good deal like a practical examination by the American Board of Dermatology and Syphilology, Inc. Because of the location, color and history, it presents a problem that involves the most profound use of good judgment. I do not think that the issue should be sidestepped. I could not get a clear understanding about the growth of the lesion. Dr Obermayer says that it has not grown. I should be inclined to leave it alone unless it does show evidence of growth or thickening. If it is taken off deep enough for one to be sure of getting rid of it, a considerable defect would be left. I should leave the removal of it to a plastic surgeon.

DR ALEX CAMPBELL (by invitation) This case reminds me very much of one reported by Dr Scharlit, of New York. His patient had stuck an indelible pencil into the skin, and shortly afterward a pigmented lesion appeared at the site. The question arose clinically as to the nature of the pigment, whether it was from the pencil or whether it was melanin. The lesion turned out to be a malignant melanoma.

DR H C L LINDSAY One is reminded of the case of a woman who had a black dime-sized plaque on her shoulder just below the left clavicle. She had a wide flat scar 2 inches (5 cm) below the black mark, which was the result of an automobile accident in which her collar bone had been broken. The black lesion being considered a tattoo mark, it was removed surgically. The color extended so deeply that it was deemed wise to have Dr A G Foord, pathologist, examine sections from this tissue. Dr Foord explained that the pigment was due to wire used in fixing the broken clavicle. The discoloration had worked to the cutaneous surface 2 inches (5 cm) above the scar on the chest over the right breast.

DR M E OBERMAYER I believe that this lesion is a simple lentigo, and the lack of increase in size over a period of two years is evidence against its being lentigo maligna. It was presented because of the interesting feature of trauma having preceded the appearance of the lesion. The patient of Dr Lindsay who had tattooing due to wire used in the fixation of a fractured bone raises the question of the possibility of an accidental tattoo. Since the skin was said not to have been unbroken by the trauma, the diagnosis of tattoo is not likely. I believe that the lesion is melanotic and—with the possibility of lentigo maligna in mind—that it should be surgically excised. Because of the cosmetically important location excision will be performed by a plastic surgeon, and I shall carry out the histologic study.

#### A Case for Diagnosis (Localized Scleroderma?) Presented by DR ROGERS F WAKEFIELD

A E B, a white man aged 32, began to have a hardness of the skin over a round patch 10 cm in diameter on the right side of the chest about eight months ago. The second similar lesion appeared three months after the first one and was located about 15 cm from the first lesion. There has been a light brown color of both lesions. After the local use of 5 per cent sulfathiazole ointment, a vesicular eruption developed, which has healed slowly.

There are round areas of induration of the skin of the right side of the chest, with some dull erythema of the margins. The deeper color at the margins gradually fades toward the middle, where the lesions are an ivory color and are thickened and brawny. There are some scarring and telangiectasia over the surfaces of the lesions.

#### DISCUSSION

DR STANLEY ANDERSON I thought that this might be a scleroderma.

DR JOHN ROGERS I agree with the diagnosis of scleroderma. The skin is definitely inelastic in the affected areas, and it has an ivory-like appearance in at least a portion of the lesions.

DR CLEMENT COUNTER I suggest the diagnosis of localized scleroderma. Carefully localized roentgen ray therapy may be beneficial. A few months ago I presented a woman having localized scleroderma on the breast. She was given six roentgen ray treatments. Each treatment was 150 r and carefully localized to the lesions. Two weeks elapsed between treatments. There were softening and improvement. On first thought, such therapy does not seem logical, especially when one considers that scleroderma is an atrophy and that the effect of roentgen therapy tends toward atrophy.

DR NELSON PAUL ANDERSON I agree with Dr Counter that this is a linear morphea. I think that it would be worth while to give the patient bismuth therapy. I have seen 3 cases of this type in which the improvement following bismuth therapy has been astounding. Two of the patients were presented before this society. One was a little girl, presented about a year ago, with a linear scleroderma involving the side of the nose. The other was a little girl with linear scleroderma involving the fingers, and improvement followed bismuth therapy. Dr J H Stokes saw the second patient and is to be credited with the suggestion of this type of therapy. A third patient, in private practice, has also improved greatly with this type of therapy.

DR ROGERS WAKEFIELD I saw this patient twice, once in May and again two weeks ago. He was sent to me in May on account of the dollar-sized patch on the front of his chest, macerated and raw, which he said had been a mass of blisters. He said that he had a pain in his chest, and he was sent to me with a tentative diagnosis of shingles. I sent him back and told the physicians who had referred him to me to continue the same treatment. The lesion stayed raw until all treatment was stopped, and then it healed. I have not seen that process occur in the localized sclerodermas, so I thought I should let it alone.

DR CLEMENT COUNTER Dr Wakefield, was there no obvious explanation for the vesicular eruption?

DR ROGERS WAKEFIELD The only explanation I thought of was that when the first eruption occurred he had been wearing a workshirt with a pencil in the pocket. Since then he has been careful not to carry anything in that pocket.

### Charcot Joint of the Right Ankle Presented by DR H C L LINDSAY

C N, a white man aged 67, had gonorrhea forty-seven years ago and syphilis thirty-six years ago. Later "tertiary ulcers" developed on the left shin. Scars of these lesions are present yet. Fourteen years ago the right foot became swollen. This swelling included the whole right leg. The present swelling of the left ankle began eleven months ago.

The patient weighs 120 pounds (54.4 Kg). He walks with a limp. The left ankle is swollen. The pupils are small and fixed. The Romberg sign is elicited.

Roentgenograms taken of the right ankle eight years ago showed a crushing injury of the tarsus, with fracture of the astragalus and of the tarsal scaphoid bone of the right foot. There is a continued destruction in the tarsal region, with resulting deformity. Some debris is present. Charcot joints are present. Roentgenograms now show the same type of disintegration of bone and cartilage as was present in the right ankle eight years ago.

The Wassermann reaction of the blood was strongly positive twenty years ago but has been negative for the past ten years.

### DISCUSSION

DR H C L LINDSAY This patient was treated with arsphenamine as early as 1908. It is to be noted that when swelling of the joint was great and some pain was present minimal changes were to be seen by roentgenograms of the bone structure. Yet in an interval of only a few weeks when swelling and pain had subsided decided disintegration of tissue, bone and cartilage was easily discernible in the roentgenograms.

### A Case for Diagnosis (Follicular Type of Seborrheic Dermatitis?) Presented by DR M E OBERMAYER and DR K L STOUT

R S, a white youth aged 20 years, who is a sailor, has had "sinus trouble" for about twelve years. His nose becomes "stuffed up" periodically, especially after sudden changes in temperature and on contact with cats. Asthmatic attacks also occur on such occasions.

The present eruption has been recurrent since the patient was 8 years old. It usually appears on the trunk. There is mild itching. Attacks last for six weeks. The lesions are bright red in the beginning of attacks and keep that shade for two weeks. Then they start to fade gradually. Physical exertion, especially if associated with excessive perspiration, seems to provoke recurrences, and it always aggravates the disorder. The eruption consists of discrete closely grouped erythematous papules. Lesions vary from the size of a pinhead to that of a pinpoint. They are distributed over the nape of the neck, the back and the upper portion of the chest and the arms. Lesions have the appearance of follicular papules with smooth surfaces. Two irregularly shaped plaques, 1 to 2 cm in diameter, denuded of surface epithelium, are present on either side of the tongue.

The biopsy section shows some intracellular and intercellular edema of the prickle cell layer in the otherwise normal epidermis. The dermis is edematous, with some lymphocytic infiltration. There is 1 large follicle, the sebaceous gland of which appears normal but whose duct is surrounded by a lymphocytic infiltrate. The sweat glands are normal.

## DISCUSSION

DR MOLLEURUS COUPERUS: I believe that the clinical appearance as well as the biopsy is compatible with the diagnosis of seborrheic dermatitis. There was much follicular plugging of the nose. The eruption disappeared at times, especially after exposure to ultraviolet radiation. I suggest the diagnosis of follicular seborrheic dermatitis.

DR HAL E. FREEMAN: Phrynoderma should be considered. This is a follicular hyperkeratosis, and I believe that a vitamin A deficiency should be thought of. I heard various members discussing pityriasis rubra pilaris. If the eruption is phrynoderma, vitamin A will help it. If it is a seborrheic dermatitis, vitamin A will aggravate it.

DR M. E. OBERMAYER: This case is difficult to evaluate. When I first saw the patient, the eruption reminded me of miliaria rubra. The associated hyperhidrosis seemed suggestive. The long duration and the microscopic features are incompatible with such a diagnosis. Follicular ichthyosis can be ruled out by the absence of signs of this disease elsewhere. The eruption is also incompatible with pityriasis rubra pilaris both clinically and histologically. Dr Couperus' suggestion of follicular seborrheic dermatitis is unlikely because of the extent of the eruption and its early onset, at the age of 8. We have no diagnosis to offer, but since an inflammatory follicular eruption is present it was thought that the administration of high doses of vitamin A might be of benefit. The patient has been taking 200,000 units a day.

**Pityriasis Rubra Pilaris** Presented by DR FLETCHER HALL

W. E., a 35 year old white man who works as a crystal grinder in a radio manufacturing plant, was well until about twelve years ago. While he was working as a musician in an orchestra, he noticed a papular eruption affecting the back of his neck and scalp. This did not respond to treatment, and within a year or so the forearms were involved. The eruption has been constant, gradually affecting more and more of the surface of the body. The legs were not severely involved until about six months ago. The patches on the abdomen are of about a year's duration. He has worked at his present job for five months. Before that, he spent seven years in a lumber mill in the Northwest. There has been no significant change in the dermatitis accompanying his change in occupation. Itching is rather severe at times but is not a constant feature.

The hypochondrium shows a patch twice the size of a palm of evenly distributed bright red follicular papules. A similar patch involves the entire lower part of the abdomen and the pubic region. The inner and posterior aspects of the thighs and the legs down to the shoe top level show similar but more pronounced follicular prominence, complicated by extensive scaling and crusting. All aspects of the forearms are similarly affected. The hands, feet, chest and back are unaffected. The dorsal aspects of the fingers have been affected but are not at present.

The biopsy specimen shows enlargement and clubbing of rete pegs without hyperkeratosis and enormous elongation and widening of the hair follicles.

## DISCUSSION

DR HAL E. FREEMAN: This is an excoriated and extremely pruritic eruption limited to the extremities, in which vesicles and pustules are present. It is typical of a dermatitis herpetiformis.

DR SAMUEL AYRES: I could not see anything that looked like dermatitis herpetiformis. I could see no classic grouped vesicles, but the patient did have a widely disseminated eruption involving the follicular structures with hyperkera-

tosis There was some scaling By looking at his arms alone one might wonder whether he was not working in cutting oils He said that the eruption was present long before he began to work at his present job I do not know whether it should be called pityriasis rubra pilaris or not It verges on the disease It is not a classic case, but I do not see any dermatitis herpetiformis I think that it comes closer to pityriasis rubra pilaris or a follicular hyperkeratosis I should like to see what high doses of vitamin A would do

DR. W. H. GOECKERMAN I have seen a good many cutaneous pictures of this type and have always had difficulty in classifying them I call this a seborrheid Pityriasis rubra pilaris or dermatitis herpetiformis do not seem logical diagnoses

DR. H. C. L. LINDSAY There are two factors here One is a chronic eczema which he has had for years, the other appears to be due to an external factor The latter is the dermatitis on the forearms and legs, extending from the lower apron hem toward the feet and from the fingers and hands to the edge of his rolled-up sleeves A percentage of men employed in polishing lenses suffer from oil and carborundum dermatitis This patient is contacting similar materials in his work

DR. NELSON PAUL ANDERSON I believe that the patient presents an atypical dermatitis herpetiformis When one looks at a relatively common cutaneous disorder like pityriasis rosea, all types of variations from the typical textbook case are found I do not see why there cannot be an atypical dermatitis herpetiformis, more or less symmetric, involving the arms and legs and anterior portion of the trunk without the classic distribution, involving the elbows, knees and upper part of the back Before I should accept any other diagnosis I should like to have dermatitis herpetiformis ruled out by differential blood counts and biopsies, particularly of the pustular and vesicular lesions It might be worth while to perform a patch test with potassium iodide, and the patient might be given some potassium iodide three times a day to demonstrate increase of lesions

DR. A. F. HAIL In closing, I must of course agree with Dr. Avers that the eruption does not look like dermatitis herpetiformis Instead of giving the patient potassium iodide as a diagnostic procedure, I shall give him vitamin A in large doses for a month and then present him again In my opinion the microscopic section looked like pityriasis rubra pilaris as described by McCarthy I am not willing to accept the diagnosis of dermatitis herpetiformis

#### CHICAGO DERMATOLOGICAL SOCIETY

Lester M. Wieder, M.D., *President*

Marcus R. Caro, M.D., *Secretary*

Nov 15, 1944

#### Pigmentation Following Morphea (and Arsenic?) Presented by DR. EARLE R. PACE

Mrs. J. L., a white woman aged 22, presents a widespread pigmentary disturbance of the neck, trunk and proximal segments of the extremities The onset coincided with the onset of menstruation ten years ago The earliest patches were in the cubital fossae and on the upper part of the inner thighs and were hard thickened and inflexible New patches have appeared from time to time, all eventually resulting in pigmentation as now seen

At present she shows coin-sized to egg-sized brown, pigmented patches which fuse into sheets in many areas The pigmentation is a smooth tan to brown discoloration flecked with lighter spots On the trunk particularly on the abdominal wall, it is diffuse and nonmargined and resembles arsenical pigmentation

The central parts of some larger patches, notably in the cubital fossae and on the thighs, show a definite atrophy, with a transparency like that seen in acrodermatitis chronica atrophicans. There is no sclerodermatous hardness anywhere now, and there are no textural changes other than this atrophy.

Three grandparents are diabetic. Both parents and two grandparents have had goiters requiring operation. The patient was potbellied in childhood and had a basal metabolic rate of 10 per cent at the onset of menstruation and the morphea. She has been under treatment by an endocrinologist in Seattle. She has taken thyroid tablets since 1934, with the exception of one year. She took 1 grain (0.06 Gm) daily between the ages of 14 and 20 and is now taking 2 grains (0.13 Gm) daily. The latest basal metabolic rate was -15 per cent. She was given solution of potassium arsenite U S P from May 1943 to May 1944, which seemed to intensify the pigmentation. The pigmentation seems to be more striking during the menstrual period.

The histologic examination of a section removed from the margin of a nonatrophic patch on the upper arm showed a flattened epidermis with a thin non-nucleated scale and a considerable amount of pigment in the basal layer. In the subpapillary layer the vessels were dilated, while the deeper part of the corium was relatively avascular. In the papillae and in the subpapillary layer there were many large chromatophores, which were densely packed with brown pigment granules. Some of these lay in linear strands along the vessels. Perles' prussian blue reaction showed a complete absence of iron pigment. Weigert's stain showed the elastic fibers to be fragmented throughout the corium.

#### DISCUSSION

DR E. M. SMITH, JR. I had a patient with scleroderma who was presented to the society some months ago in whom there was the same degree of pigmentation. That patient did not receive any arsenic and improved remarkably well on bismuth therapy.

DR THEODORE CORNBLEET. The bones have been found to act as major depots for arsenic. From them this element is distributed and then returned via the blood. Considerable quantities can be present in such a circulation, even though little is excreted by the urine, feces and sweat some time after incorporation into the body. The agents which mobilize lead and calcium may be useful for mobilizing arsenic. Thus parathyroid is excellent for a while, until it becomes ineffectual by habituation. If stopped for a while, it may again be employed successfully. Dihydrotachysterol has not proved so effective as parathyroid thus far. Sodium citrate, which is useful in chronic lead poisoning, is definitely useful. These agents I have found worth while against arsenical keratoses and pigmentation.

DR C. W. FINNERUD. Although the patient may have misunderstood my question, she gave me the impression that she thought that if any change had occurred there was less pigmentation after she had taken arsenic and that in the beginning there was not only greater pigmentation in the areas but also notable hardness.

DR EDWARD A. OLIVER. I had the opportunity of seeing and examining this patient in my office. After listening to her history carefully, I felt that the pigmentation, even though it appears to occur in localized areas, was due to the ingestion of arsenic. She undoubtedly had morphea and was given solution of potassium arsenite U S P, which she took for over a year.

DR S. J. ZAKON. Why would not sodium thiosulfate be indicated as a therapeutic agent after arsenic?

DR E. R. PACE. As to the effect of arsenic, the patient originally told me, or at least I understood it so, that the pigmentation was intensified by arsenic. That was also the impression that was given by another physician who had her under observation. Since then I asked her the same question, and she said that it was not increased by the arsenic. I saw her only twice.

**A Case for Diagnosis (Lichen Planus?)** Presented by DR F E SENLAR and DR M R CARO

J Z, a white woman aged 39, first noticed a white spot "like a canker sore" on the left side of her tongue about one and one-half years ago. This spread rapidly to involve the buccal mucosa of the left cheek. The entire tongue soon became inflamed, and there was considerable pain. Occasional slight remissions were followed by sudden exacerbations. Smears of material taken from the tongue by a physician consulted previously were reported to have shown yeast spores, and a roentgenogram of the lungs showed a peculiar shadow, that was not diagnosed.

When the patient was first seen by us, on March 15, 1944, the condition of the mouth was approximately the same as it is today. The patient also complained of a vaginal discharge and a productive morning cough. There were a few lesions on the back of the left hand that suggested lichen planus.

Smears of material from the tongue and buccal mucosa showed no fungi. The urinalysis and chemical and cytologic examinations of the blood gave normal results. The fluoroscopic examination and the roentgenogram of the chest showed massive irregular density in the middle of the right pulmonary field and multiple nodular infiltrations in other parts of the lungs. These conditions were considered consistent with a mycotic infection. A bronchoscopic examination showed the laryngeal mucosa to be ulcerated in a manner similar to that of the tongue. The trachea and bronchi were essentially normal. A slight amount of secretion was aspirated for examination, but no fungi or other organisms were isolated.

The patient had many amalgam and gold fillings in her teeth. All the amalgam was removed from her mouth, to rule out a possible galvanic current as an etiologic factor in the production of the stomatitis. There was no improvement in the lesions or in the symptoms following this procedure.

A specimen was removed from her tongue for histologic examination and was reported as follows: "The surface epithelium is missing and is replaced by a fairly thick membrane composed of debris, fibrin and numerous leukocytes. The superficial layers of the tongue itself are infiltrated by a mixture of leukocytes and lymphocytes and a moderate number of histiocytes. There is a decided new formation of capillaries, and in places the infiltrating cells tend to assume a somewhat perivascular arrangement. There is considerable destruction of normal tissue, including striated muscle tissue. A diagnosis of acute and chronic non-specific inflammatory granuloma of the tongue was made. There was no histologic evidence of tuberculosis, actinomycosis or blastomycosis. With this microscopic picture syphilis should be ruled out."

Biopsy of a specimen taken from a lesion on the back of the left hand showed the histologic changes of lichen planus.

Before coming under our care, the patient had received many forms of treatment, including injections of arsenic, mouth washes and local cautery. Since then, in addition to dental care, she has received vitamin B complex by mouth, injections of a bismuth preparation, injections of mercuric salicyarsonate and intracutaneous injections of smallpox vaccine. In spite of the treatments, there has been no appreciable improvement in the condition of the mouth or in the pain.

At present there are healing papules of lichen planus on the backs of the hands and on the flexor surfaces of the left wrist and forearm and a papule on the left thigh. The left buccal mucosa is eroded and inflamed. There is a large ulceration on the left side of the tongue, covered by a grayish membrane and a smaller ulcer in the midline. In addition, there are whitish patches on the dorsal surface of the tongue.

**DISCUSSION**

DR C W FINNERUD: It is known that lichen planus can closely simulate lupus erythematosus in all areas and vice versa. I saw the section, and I must say that the section taken from the dorsum of the hand is an excellent specimen of lichen planus. If she had only those lesions on the hands I am sure it would



be decided definitely that the patient has lichen planus. The changes present on the lower lip were not characteristic of lupus erythematosus. I think that it is altogether likely that she has lupus erythematosus, because of the erosions on the buccal mucous membrane with little vessels which radiate out from the border, one of the characteristics of recent lesions of lupus erythematosus of the buccal mucous membranes, however, I have never seen erosion so severe in lupus erythematosus as in this instance. This is one of the symptoms which is usually absent in lichen planus. I think that this case will prove to be one of lupus erythematosus.

DR C W LAYMON, Minneapolis. Erosion or ulceration is most unusual in lichen planus, but it does occur. Such cases have been reported in the French literature, and in one instance an epithelioma developed at the site of such an ulceration. In the case of Drs Senear and Caro, I think that the diagnosis of lichen planus should be accepted, especially in view of the presence of lesions on the body.

DR OLIVER S ORMSBY. The erosion on the tongue interested me. My associates will agree with me that we have had 5 or 6 patients in the office with erosions similar to this, produced by lichen planus.

DR H E MICHELSON, Minneapolis. With patients who have severe lichen planus in the mouth the cutaneous lesions may subside but the oral lesions persist for years. In such patients heavy metals may precipitate stomatitis, and a patient may become ill from this.

DR F E SENEAR. I am particularly glad that Dr Finnerud brought up the question of lupus erythematosus. When we first saw this patient we considered diagnoses of lichen planus, lupus erythematosus and monilial infection of some type. One thing that was striking in the picture was the presence on the dorsum of the tongue of a number of tiny lesions, of pinhead size to slightly larger. Many of these cleared at the center, giving the appearance of tiny reddish stomas surrounded by a fine whitish ring. This patient had this the first day we saw her. The palate was heavily involved, presenting the same type of lesion. It is said that erosion or ulceration may occur in lichen planus of the mucous membrane, yet we have never seen breaking down so extensive as that in this case. The biopsy had been made on a specimen from the tongue at another institution. We were unable to get another biopsy, and the report on the biopsy as sent to us was not at all satisfactory.

### **Perifolliculitis Capitis Abscedens et Suffodiens, Cleared with Penicillin**

Presented by DR THEODORE CORNBLEET and DR M S KAGEN (by invitation)

This patient has had an eruption of the scalp for one and one-half years, which consisted of large, burrowing intercommunicating sinuses filled with pus and covered by crusts. The hair was absent over the affected areas. Various medicaments were used, without benefit, including sulfonamide drugs administered locally and internally and roentgen rays.

In September the patient was hospitalized and received 75,000 units of penicillin intramuscularly and local applications of the solution. The latter was in a concentration of 200 units per cubic centimeter of isotonic solution of sodium chloride and was used for five days. There was prompt improvement on the regimen, but complete healing did not occur until a few weeks ago.

### **DISCUSSION**

DR H E MICHELSON, Minneapolis. I had experience with 2 such cases in which I used penicillin. My first impression was that the patient was doing well. After a week or two the lesion appeared to fill up again. Penicillin does serve to clear up the lesions, but they recur. I did not use it locally.

DR THEODORE CORNBLEET. Workers with experience in the use of penicillin stress that a proper dosage schedule must be worked out for each disease in which this remedy is useful. It is possible in some dermatologic cases that local use of the drug may bring results that surpass the limited ones possible from its systemic

use At any rate, in this patient the injections and local use of penicillin brought gratifying results None of all the other remedies previously tried, including the sulfonamide compounds, helped The alopecia is permanent The result in this patient suggests the use of the same drug against such entities as acne conglobata and pyoderma faciale and perhaps sycosis barbae

DR C W LAYMON, Minneapolis One of the cases to which Dr Michelson referred was a case of acne conglobata in which 1,200,000 units of penicillin were administered within approximately a week Although the immediate response was gratifying, the patient had a relapse within six to eight weeks Another similar course of penicillin was then given, with indifferent results

**A Case for Diagnosis (Psoriasis?)** Presented by DR THEODORE CORNBLEET and (by invitation) DR DAVID COHEN and DR H C SCHORR

J G, a Negro woman aged 62, has a generalized eruption, of six years' duration, which began on the left leg after a burn Blisters then appeared and have recurred from time to time This generalized eruption has occurred each spring She was hospitalized on Aug 18, 1944 There has been a generalized dry, scaly dermatitis with fairly sharply outlined patches on the backs of the hands and feet The face was involved but now is cleared The palms and soles are uninvolved There is moderate itching

The urine was normal Determinations of the blood chemistry showed non-protein nitrogen 20 mg per hundred cubic centimeters of blood, total protein 7.4 Gm, albumin 4 Gm and globulin 3.4 Gm per hundred cubic centimeters of blood

The histologic examination of a section removed showed changes characteristic of psoriasis

DISCUSSION

DR RUBEN NOMLAND, Iowa City I believe that this woman presents some sort of lymphoblastoma The microscopic picture, I thought, was compatible with the early infiltrating stage of mycosis fungoides There was acanthosis with cellular infiltration in the upper part of the cutis Clinically, I believe that it also belongs in the group of lymphoblastomas rather than that of psoriasis, which is extremely rare in Negroes

DR THEODORE CORNBLEET This patient's lesions have changed considerably from time to time At one time there was more than a superficial resemblance to pemphigus foliaceus After this, the skin assumed a normal appearance under treatment with indifferent materials There has been some question about arsenical medication She received none from us, and no evidence of arsenic was found in the urine, hair or nails Some form of lymphoblastoma must be considered seriously Neither her blood nor her marrow, obtained by sternal puncture, indicates this thus far There are no lesions present suggestive of psoriasis except on the right hand The changes visible in the biopsy sections bear a considerable resemblance to the histologic changes found in psoriasis, but there are additional features in the slide that were pointed out to me which are not in keeping with those of psoriasis I mentioned psoriasis as a point of departure for our discussion I do not know what the diagnosis is

**Favus** Presented by DR L F WEBER and (by invitation) DR C H STUBEN-RAUCH JR

J M, a married woman aged 24, a resident of Chicago all her life, has had an eruption on her scalp for seventeen years The top of the scalp shows alopecia and diffuse scaling The scales are adherent and yellowish The hair in the involved areas is brittle and lusterless There are only a few fractured hairs in the involved areas The skin shows atrophy The infected hairs showed a gray fluorescence under the filtered ultraviolet rays Some of the hairs removed for microscopic examination showed large spores occurring in chains within the hair substance Air spaces were noted within the hair The examination of the scales

attached to the hairs showed a mass of hyphae. Sufficient time has not elapsed for the cultural growth to show the primary colony.

The patient has had an ill defined patch of redness on the right arm. The microscopic examination of scrapings removed from the right arm showed no fungi.

#### DISCUSSION

DR S W BECKER. Clinically, this patient presents tinea amiantacea, a condition described by Dr Muir and me (Becker, S W, and Muir, K B. *Tinea Amiantacea*, ARCH DERMAT & SYPH **20** 45 [July] 1929). The nature of the disease is uncertain. It has occurred in association with psoriasis of the scalp, and I have seen it once in association with tinea capitis caused by *Microsporon audouinii*. The hairs are matted to the scalp in scales, and as the hair is elevated the scales are split in a manner suggesting the splitting of fibers of asbestos. I could see no spores in the hairs. The patient has a scar on the vertex, the nature of which she is not sure of. There are no scutula, as should be seen in favus. The therapeutic test for tinea amiantacea can be carried out quickly, since it responds readily to an application of 5 per cent ammoniated mercury ointment.

DR M H EBERT. I agree with Dr Becker. This is clinically the disease first described by Dr Becker in this country as tinea amiantacea. I have seen a number of these cases. I think that the use of ammoniated mercury is an ideal one to differentiate favus. I wonder whether the other gentlemen who studied this case might possibly have been able to find favus hyphae in the hairs. I did not see any.

DR MAURICE OPPENHEIM (by invitation). Favus does not resemble the presented case, there are no scutula with the yellow color and scattered scars visible and no clusters of hairs between the scars. The scarlike spot in the temporal area is a congenital atrophy of the skin, aplasia cutis congenita, as described by Voerner. My diagnosis in this case is *Trichophytra capilliti*.

DR L H WINER, Minneapolis. I agree with Dr Becker that this is not favus but tinea amiantacea. I do not recall that any one has found fungi in tinea amiantacea. I get good results by treating these patients with 5 per cent ammoniated mercury ointment. In favus, the fungi are easily found, since the scutula are formed by scales which teem with spores and hyphae.

DR F E SENEAR. I understood that this disease took its name from splitting of the scales. I should like to ask Dr Becker about the derivation.

DR S W BECKER. "Amiantacea" means "asbestos-like." The splitting of the scales on elevation of the hair reminds one of the splitting of asbestos hence the name.

DR H M HEDGE. In a case of a disease of seventeen years' duration, it might also be expected that some lesions should be found in the finger nails if it were favus. That would be due to scratching of the head with the finger nails. I did not find lesions in the finger nails.

DR L F WEBER. I am sorry that not every one agrees with our diagnosis of favus. The patient's scalp shows diffuse superficial but adherent scaling, with alopecia and atrophy. There was some resemblance to seborrheic dermatitis, but it was not this disease. The hair shaft showed sausage-shaped spores, which are like those found in favus. Several members did not devote enough time to the microscopic specimen, and that is the reason they failed to see the spores.

Cultures were made, and Dr Neuhauser, a few minutes before the discussion, stated that the primary colony had developed sufficiently to be recognized as favus. I thought that three weeks was the usual period required for growth, but Dr Mitchell has made a good point that it takes six weeks in some instances.

The patient's husband and son are without signs of favus. It is remarkable to find one member of the family affected, unless extraordinary pains are taken, such an experience is exceptional in the present epidemic of ringworm.

I do not agree with Dr Hedge that involvement of the nails with favus must follow if this disease is on the scalp

**A Case for Diagnosis (Mycosis Fungoides)** DR DAVID V OMENS and (by invitation) DR HAROLD D OMENS

A K., a Jewish merchant aged 47, a widower, presents an eruption of eight years' duration, accompanied with variable degrees of itching

On the body and extremities are numerous variable-sized, irregularly shaped patches of infiltration, of a smoky or violaceous color, some of which are actively inflamed while others are quiescent but all of which present scaling of a fine character. The eruption seems to improve during the summer months, almost to complete disappearance except for pigmentation which remains in the involved areas. The treatment over this length of time has consisted of application of various salves and numerous roentgen ray treatments without clearing of any of the lesions at any one time.

The family history reveals that a younger brother died of carcinoma of the rectum at the age of 26 years, and the patient's wife died four years ago of sarcoma of the hip.

The histologic examination of a section removed showed areas of parakeratosis of the stratum corneum, with areas of increased width of the stratum granulosum, edema of the prickle cell layer, which was intercellular and intracellular, some spongiosis and pronounced uniform acanthosis with branching or daughter cones of the rete. The papillae were elongated and bulging at their tips, they were edematous, and the blood vessels were dilated and the suprapapillary plates were thinned to two or three rows of prickle cells. The subpapillary portion of the cutis was edematous and presented an infiltrate which was perivascular and somewhat suggestive of a polymorphonuclear cellular infiltrate.

#### DISCUSSION

DR C W FINNERUD. I did not think that it was mycosis fungoides for several reasons. My first thought was that it was generalized neurodermatitis. My second thought was that it was parapsoriasis en plaques.

DR OLIVER S ORMSBY. I do not believe that a positive diagnosis can be made today. I had an illuminating example like this many years ago. The patient had scaling plaques that were considered parapsoriasis. He even consulted Dr Brocq, in Paris, who described the en plaques types of parapsoriasis. Brocq told him that it was parapsoriasis. We observed the patient for several years, and mycosis fungoides eventually developed. Our patient had considerable itching, which is unusual in parapsoriasis. The patient presented today had a good deal of itching. That would be against a diagnosis of parapsoriasis. I think that a period of observation will be necessary to place this case definitely.

DR HERBERT RATTNER. I saw this patient three years ago, at which time I made a clinical diagnosis of mycosis fungoides. The clinical picture has not changed since then.

DR RUBEN NOWLAND, Iowa City. I believe that the microscopic section showed the early infiltrating stage of mycosis fungoides, just a borderline change. It may be a good many years before clinical infiltrating plaques develop. I have seen 1 such case, in which mycosis fungoides took eight or ten years to develop.

DR L H WINER, Minneapolis. I am in accord with Dr Montgomery's opinion that definite parapsoriasis usually remains parapsoriasis, whereas diseases like this which are questionably parapsoriasis are really mycosis fungoides from the outset. The essential thing is that the microscopic section must be examined closely to see that the infiltrating cells are really reticulum cells, whereas in parapsoriasis there is more disintegration of the epidermis. The infiltration in parapsoriasis goes right up to the epidermis, and the epidermis-cutis border cannot be seen clearly. In this case the infiltration is really a proliferation of the cells.

around the blood vessels. Disappearance of the lesions at times is one of the characteristics of mycosis fungoides. The reticulum cells undergo liquefaction necrosis and disappear spontaneously.

**Acrosclerosis (Sellei)** Presented by DR EDWARD A OLIVER and (by invitation) DR ARTHUR GREENBERG

The patient, a white man aged 54, by occupation a salesman, states that about ten years ago his ears became painful as a result of small whitish crusts which appeared on the cartilage of each ear. When these crusts were picked off, small, pinhead-sized ulcers resulted, which would again form a crust, a cycle which has been active to the present. From that time to the present his upper and lower extremities have been unduly sensitive to cold as never before.

After being confined to bed with pneumonia two years ago, he noticed that his hands and forearms were becoming stiff and his finger tips were painful to slight pressure. He had all his teeth extracted two years ago and never realized that his face was drawn until the fact was brought to his attention recently. He does not know when the small white spots appeared on his chest. He has never had difficulty in swallowing.

When the arms are raised, the hands and fingers blanch, they become somewhat cyanotic in the dependent position. The skin over both hands and forearms is smooth, waxy, atrophic and inelastic. The fingers of both hands are held in a semiflexed position. There are crusted necrotic areas over the tips of some of the fingers. There is decided involvement of the ears, chin and tissues of the cheeks, giving the patient a rather drawn appearance. There are multiple depigmented spots on the anterior thoracic wall.

The results of urinalysis and the blood count were normal except for a moderate leukocytosis due to existing infection in one of the fingers. The Kahn reaction was negative. Determinations of blood chemistry showed urea 14.6 mg per hundred cubic centimeters, creatinin 1.5 mg, sugar 90.5 mg, chlorides 511.5 mg, calcium 13 mg and phosphorus 2.7 mg.

#### DISCUSSION

DR CARL W LAYMON, Minneapolis. Ever since Sellei's first reports concerning acrosclerosis, about twelve to fifteen years ago, there has been considerable debate about the disease. Sellei defined acrosclerosis as a disease characterized by shrinking and contracture of the skin, arising always symmetrically on the hands and feet and on the face at the same time and accompanied with pallor, cyanosis and pain on exposure to cold. This definition, however, is not essentially different from that of diffuse scleroderma, and I do not believe that it deserves the distinction of being regarded as a separate entity. Sellei also confused the nomenclature by labeling extensive morphea "scleroderma diffusum." Sellei further caused confusion by calling bandlike forms of scleroderma involving the hands "sclerodactylia."

DR MAURICE OPPENHEIM (by invitation). I agree that acrosclerosis is a part of scleroderma. I have never seen a case of acrosclerosis isolated without diffuse scleroderma. Scleroderma starts on the extremities and spreads to the face, and the same thing is true of sclerodactylia or acrosclerosis. I do not believe that it is right to separate acrosclerosis from diffuse scleroderma. The designation "acrosclerosis (Sellei)" should disappear.

DR EDWARD A OLIVER. I had hoped that this case would produce considerable discussion. Unfortunately, Dr O'Leary is not here. This case appeared to me to be a fairly typical example of what Sellei described as acrosclerosis. The disease affects women chiefly. The patient shows a typical facial sclerosis. The skin of the face is drawn, stretched and taut, the lips are drawn and radially furrowed, the fingers are stiff and shrunk, and there is ulceration of the terminal phalanx of one finger. The chest and arms are not affected, and the patient complains of

symptoms in the hands and fingers similar to those experienced by a patient with Raynaud's disease. I am entirely neutral on the subject, but this case appears to me to differ considerably from the typical picture of scleroderma and sclerodactylia.

**Scrofulous Gummas** Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS

C. P., a schoolboy aged 16, presents several broken-down areas which are in the process of draining. The first one appeared as a single pigmented nodule four months ago, broke down and drained and shortly afterward was followed by other lesions in the immediate vicinity. Eighteen months ago bilateral walnut-sized swellings developed in the neck, the one on the right side breaking down and draining for about five months and then gradually healing. One year ago an egg-sized swelling developed on the angle of the right jaw, which was incised, drained for some time and is now in the process of healing.

This boy has lived in Chicago all his life. Four years ago he was hospitalized for eight months in the City of Chicago Municipal Tuberculosis Sanitarium for a spot in the right lung. The sputum and the roentgenograms were always negative for tuberculosis. He was discharged as cured. Two years ago while in Tennessee for three weeks he drank unpasteurized milk.

The Mantoux test (1:10,000) was strongly positive. The Kahn reaction was negative. A smear from a lesion revealed many diplococci on the Gram stain. The Ziehl-Neelsen stain of a section was negative for tubercle bacilli.

Biopsy revealed absence of the stratum corneum, with widening of the stratum granulosum and acanthosis of the prickle cell layer with corresponding elongation of the papillary bodies, which were edematous; the cutis was edematous and rich in blood vessels which were engorged and with a perivascular cellular infiltrate composed of lymphocytes, leukocytes and plasma cells. In the deepest portion of the cutis were areas of necrosis around which were epithelioid cells which were surrounded by lymphocytes. Leukocytes and giant cells were only sparingly present.

The roentgenographic examination showed the cardiothoracic ratio well within normal limits. There was a bilateral increase in the hilar markings, with some peribronchial infiltration extending into the left infraclavicular region. There was also a diffuse, slightly increased density in the upper two thirds of the left pulmonary field. These conditions were compatible with an old tuberculosis and pleural thickening.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis. I prefer the term "tuberculosis colliquativa" for when the term "scrofulous gumma" is used it carries certain implications of similarity to syphilis, which are unnecessary with the use of the other term.

DR. EDWARD A. OLIVER. I do not think that this type of tuberculosis is so rare as it might be thought. When Dr. Finnerud and I were on service at the Children's Memorial Hospital we saw several cases. I presented 1 patient years ago, a youngster of about 10, with numerous gummas on the back and shoulders.

DR. L. H. WINER, Minneapolis. This form of tuberculosis, although not closely similar histologically to the regular forms of tuberculosis of the skin, shows a definite picture, that is, that there is reticulation of the connective tissue much like a lace curtain. In the holes of this reticulation are implanted nests of plasma cells. In addition, nests of giant cells are found, which were so characteristically shown in the slide.

**Disseminated Miliary Sarcoid (Boeck)** Presented (by invitation) by DR. MAURICE OPPENHEIM

Mrs. T. S., a white woman aged 47, presents on the shoulders, on the trunk to the girdle and on the lower extremities many groups of round and oval

nodules and papules from the size of a hempseed to that of a pea. The papules are brown and yellowish, have little scales and are mostly in clusters surrounding a bigger, flat, yellowish papule or a slightly pigmented area. The clusters simulate syphilis corymbosa, a diagnosis which was made previously. There is a decided infiltration, and the diascopic examination shows grayish yellow foci, as in lupus vulgaris. The clusters vary in size from that of a walnut to that of a child's palm. There are no single nodules or papules. The mucous membranes, palms and soles are free. There is no lymphadenopathy. No itching is present. The disease started one year ago on the legs and spread gradually over the entire body. The general health of the patient is good.

The results of laboratory examinations were all negative. The patient is now being treated with acetarsone in the same way as I recommend for pemphigus chronicus.

The histologic examination of a section removed showed a normal epidermis and the papillae flattened on the areas where the infiltration extended to the papillary layer. The infiltration was formed by round or more irregularly shaped clusters of epithelioid cells and a few giant cells. Some of these clusters had a border of lymphocytes at the periphery. There was no caseation. In some foci the epithelioid cells were the only cellular elements. The single clusters which were located in the reticular layer of the cutis were in some districts located in the stratum subpapillare and the stratum papillare. The subcutis was not involved.

#### DISCUSSION

DR RUBEN NOMIAND, Iowa City. I think that this case is typical of sarcoid. When I was in Chicago, I was interested in the relation of this disease in white and Negro persons and whether it should be called sarcoid when occurring in the Negro or whether it was a different disease. I think that it is still open to question. Sarcoid in the Negro, in my opinion, is different from sarcoid as seen in white persons.

DR H. E. MICHILSON, Minneapolis. There is not a great deal to discuss about this patient. I heartily agree with the diagnosis, and I can only point out that, even though there is a considerable superficial involvement, the woman is in excellent health, which probably indicates that no vital internal organ is involved.

DR C. W. FINNERUD. This is a beautiful demonstration. I do not see how any one can differ with the diagnosis.

DR MAURICE OPPENHEIM (by invitation). I do not want to talk about the etiologic factors, in this case there is no tuberculosis of the lung. I do not believe that tuberculosis is the only reason for sarcoid. The clinical aspect is peculiar because of the grouping and the corymbiform aspect. She has been suffering for one year. The 2 cases of sarcoid in Negroes which I have seen in my clinic were instances of sarcoid of Boeck of a small nodular type.

#### A Case for Diagnosis (Erythema Multiforme Bullosum?) Presented by DR CLEVELAND J. WHITE

Baby S was born Sept. 16, 1944, weighing 8 pounds 4½ ounces (3,756 Gm). At birth, bullae were present on his index fingers and thumbs. Eighteen hours later there were two large collapsed bullae, with erythematous bases, on the dorsal areas of the small fingers of both hands and a small erythematous lesion on the forehead. There was no fever. He was given 3,000 units of penicillin every two hours for forty-eight hours.

On September 17, toward evening, bullous lesions appeared about the eyelids. The finger nails were yellowish and appeared softened. On September 19, the baby began taking nourishment. A few new lesions were noted on the back. The culture revealed nonhemolytic staphylococci.

On September 21, there was a further spread to the right scapular area, consisting of flat, slightly depressed, ulcerating lesions, 5 mm in diameter, with

yellowish, dry crusts on the surface. There were slightly erythematous areolas about the lesions. There was no evidence of bullae at first. Another lesion was noted on the right side of the abdomen. The Nikolsky sign has not been present.

On October 9, administration of 2 per cent solution of gentian violet medicinal was started, and the baby was given vitamins D and C, 50 mg daily, and vitamin B complex. On October 13, a transfusion of 90 cc of blood was given. Lesions were developing on the toes. On October 25, the throat was injected and there were bullae in the oral cavity. There were a few new bullae. The baby was not taking the formula well and was regurgitating the feedings. On October 27, there was a bullous formation in the throat with sloughing. Later in the day he had considerable respiratory difficulty, requiring aspiration of the throat.

On November 7, a phytotoxic test was indicative of a toxicoderma suggestive of erythema multiforme bullosum, this clinical opinion was expressed by Dr Oliver, who saw the baby in consultation.

The transfusions were repeated. The baby has had an intermittent rise of temperature to 102 to 103 F, beginning approximately three weeks after birth.

The blood was examined on three occasions, with the following results:

On September 22 examination showed 4,810,000 erythrocytes, hemoglobin content of 14.5 Gm, and 8,450 leukocytes, with 40 per cent polymorphonuclears, 51 per cent lymphocytes, 4 per cent eosinophils and 5 per cent monocytes.

On September 24 there were 5,520,000 erythrocytes, hemoglobin content of 16.5 Gm and 17,600 leukocytes, with 56 per cent polymorphonuclears, 42 per cent lymphocytes and 2 per cent monocytes.

On October 30 the blood showed 3,850,000 erythrocytes, a hemoglobin content of 10.5 Gm and 13,200 leukocytes, with 48 per cent polymorphonuclears and 52 per cent lymphocytes.

The mother is 27 years old and in good health. She was seen several times during her pregnancy, and nothing abnormal was found. The father, 30 years old, has a cataract of the left eye. There is no family history of tuberculosis, cancer, syphilis, diabetes or blood dyscrasia. The mother has had five children. The first, a boy born in 1935, died of a ruptured appendix at the age of 4½ years. The second, a girl born in 1936, died of "pemphigus" one month after birth. The third, a boy born in 1939, had a bilateral inguinal hernia at birth, he is living and well. The fourth, a boy born in 1941, died of "pemphigus" twenty-nine days after birth. The fifth child is the subject of the report.

At the present time, November 15, the baby is marasmic and near death.

#### DISCUSSION

DR S. J. ZAKON: If the bullae appeared at birth, a diagnosis of dermatitis exfoliativa neonatorum (Ritter's disease) should be considered. Penicillin is responsible for the fact that the child is still alive. The majority of such patients usually die in a few days.

DR CLEVELAND J. WHITE: Because of the history, the mother was examined several times before delivery and nothing could be found. I saw the baby immediately after birth, and the lesions were present. Dr Oliver was kind enough to examine the baby. He thought that possibly the lesions belonged in the erythema multiforme bullosum group.

DR EDWARD A. OLIVER: The interesting feature of the case to me was the mother's history. This was the fifth child, and three of them had the same type of eruption at birth. The lesions suggested a type of bullous multiform erythema. I recalled a case which Dr Michelson showed once at the annual meeting of the American Dermatological Association. He showed a photograph of a fetus with definite symptoms of erythema multiforme.

DR F. W. LYNCH, St Paul: There is obvious difficulty in making a diagnosis from a photograph. Several lesions appear to be umbilicated and call to mind the case mentioned by Dr Oliver, in which the later diagnosis of vaccinia was based on histologic study by Dr Michelson. I reported the case in 1932 (Derma-



tologic Conditions of the Fetus, with Particular Reference to Variola and Vaccinia, ARCH DERMAT & SYPH **26** 997-1019 [Dec.] 1932) In Dr White's case I think that microscopic examination is needed for certain diagnosis. In Dr Michelson's case the diagnosis was intrauterine pemphigoid vaccinia. The mother was vaccinated during pregnancy, and, as a result, the vaccine was transmitted to the fetus and the baby was born dead, with the eruption. In Dr White's case I think that the diagnosis might be approached in this manner. An external infection of this appearance and course would probably have to be a form of pyoderma, and in that case it should have responded to therapy with penicillin. With systemic infection resulting in so early an appearance of an eruption, one would think that the infection must have been acquired in utero. Such infections are rare, and in my rather complete review of the literature in 1932 I did not discover reference to a picture such as this. As suggested by Dr White, erythema multiforme must be considered, but the eruption should not have persisted for two months with so little change in appearance. I doubt that diagnosis in this case. Nevus, new growth or ordinary metabolic disturbance fails to explain such an eruption. Thus I am led to conclude that the infant has a congenitally defective skin, and I should regard the case as an example of severe epidermolysis bullosa.

DR L. F. WEBER: What about a persistence of the epithelial layers?

DR F. W. LYNCH: The older literature on persistence of the epithelial layers is confusing, with few satisfactory microscopic studies. Such eruptions seem never to have bullous elements, many are confused with ichthyosis and simple maceration, and others may be embryonic evidence of earlier evolutionary forms.

DR RUBEN NOMLAND, Iowa City: I believe that the last diagnosis Dr Lynch mentioned, epidermolysis bullosa, is the correct one. The family history and the blisters at birth are in favor of such a diagnosis. I had a case similar to this, that of a child, and at necropsy there was complete separation of the entire epidermis from the dermis.

DR CLEVELAND J. WHITE: The discussion has brought out many important points concerning this unusual case. I appreciate the fact that a biopsy should be performed, but permission to do so has not been obtained. The different diagnoses suggested, of course, bring up again the question of whether the eruption is of the erythema multiforme group or is epidermolysis bullosa or pemphigus neonatorum.

All forms of treatment have been used, including administration of penicillin. The latter has probably postponed the fatal issue, as suggested by Dr Zakon.

NOTE—The baby died six days after presentation of the case. The postmortem examination of the viscera was essentially noncontributory. A biopsy of an active lesion was made before death, and the sections were compatible with the diagnosis of epidermolysis bullosa.

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Reuben Friedman, M.D., *Secretary*

Nov 17, 1944

#### A Case for Diagnosis (Lupus Erythematosus, Seborrheic Dermatitis?). Presented by COMMANDER H. E. TWining (MC), USNR

J. S. D., a white man aged 56, who has never been seriously ill, presents on the chin chronic erythematous, sharply demarcated, papular lesions. On the face and ears there are pronounced erythema and scaling. On the cheeks there are several small plaques. The scalp is partially covered by silvery white scales. About two and a half years ago erythematous vesicular and papular lesions developed on the upper lip and on the chin. Since then there has been a gradual spreading of the eruption, which now involves the face, scalp, ears and eyelids.

The Mantoux reaction, cultures for fungi and repeated Kahn reactions of the blood for syphilis were negative. The blood sugar level, complete blood count and results of urinalysis were within normal limits. A roentgenogram showed that the chest was normal.

The patient has been given oxophenarsine hydrochloride (mapharsen), bismuth preparations, gold sodium thiosulfate, roentgen ray therapy and topical applications containing at various times sulfur, mercury, salicylic acid and penicillin. He was presented before this society in 1943.

#### DISCUSSION

DR CARROLL S WRIGHT: The appearance of this man's tongue suggested a decided vitamin deficiency. The studies of Dr Sullivan, in Baltimore, and some studies that have been made here indicate that seborrheic dermatitis may also be associated with vitamin deficiencies, particularly pyridoxine and riboflavin. I believe that this patient has a pronounced seborrheic dermatitis and probably also an old sycosis vulgaris. I would suggest that he be given intravenous injections of a vitamin B complex preparation which has a fairly adequate content of riboflavin and other vitamin B factors. He should receive local therapy for the seborrheic dermatitis. Brewers' yeast and other orally administered vitamin preparations should be prescribed.

COMMANDER H E TWining (MC), USNR: I do not know how many members can recall this case, which was presented about a year ago. The patient then had lesions only on the upper lip and on the chin. The question was whether he had lupus erythematosus, sycosis vulgaris, syphilis or seborrheic dermatitis. Disregarding the negative serologic reactions of the blood, I treated him with a bismuth preparation and oxophenarsine hydrochloride and later with gold sodium thiosulfate. He has also had multiple vitamin therapy. His condition, however, has gradually grown worse, with involvement of the scalp. At no time has there been any exudation associated with this process, the lesions have always been dry. All treatment so far has been ineffectual.

DR WILLIAM E EHRLICH (by invitation): How much clinical study is being done on these cases? Would it be worth while to study the patient for the presence of the Libman-Sacks syndrome or to look for tuberculosis of the kidneys? Are the lymph nodes generally enlarged? Are there other signs and symptoms which are generally found in cases of lupus?

**Purpura Annularis Telangiectodes** Presented by DR CARROLL S WRIGHT and DR E R GROSS

Mrs F H, a white woman aged 27, presents on the lower extremities patches of red telangiectatic puncta. The color does not fade on pressure. There is a slight tendency to pigmentation in some of the patches. Four months ago the patient noticed red spots on the legs. These gradually increased in size, and the color deepened. There are no symptoms. In the last three weeks (from October 25 to November 17) the eruption has spread tremendously, with extreme pigmentation almost covering the original patches on the lower parts of the legs.

#### DISCUSSION

DR FRED D WEIDMAN: A good many years ago Dr Arnett and I reported a case something like this, in which, too, the diagnosis swung between possible Majocchi's disease and something else. We finally concluded that it was a case of unusual purpura. In our patient, a young woman, the disease eventually became more extensive. First, it began on the lower extremities, as in the case tonight. Histologic studies were made, the reactions of the blood for syphilis were negative, and the coagulation time, the platelet count and the sedimentation rate were normal. That is, the usual exhaustive studies indicated in a case of purpura were made, and finally it was decided that it was a case of purpura of unknown

derivation A number of years later the patient married, and the cure for her idiopathic purpura was pregnancy

DR SIGMUND S GRFENBAUM I agree with the diagnosis

DR CARROLL S WRIGHT When I was in medical school I roomed with a medical student who had the same disease as the patient here has He was seen by Drs Udo Wile and Fred Wise and two or three other specialists who were at Ann Arbor, Mich, at the time, all of whom made the diagnosis of Majocchi's disease No treatment was administered, and his purpura also disappeared in about two years and has never recurred

**Dermatofibroma Protuberans** Presented by DR SIGMUND S GRLENBAUM and DR SIMON KATZ

J C J, a white man aged 62, of good general appearance, presents over the lumbosacral region a number of nodular, elevated, keloid-like growths The area is purplish red in color and is about 8 by 5 cm in diameter It is hard and fibrous and not tender It presents moderate telangiectases A small ulcer is present on the lower portion of the lesion In 1912 a furuncle developed over the lumbosacral region, which lasted for two months An elevated and firm scar about 0.5 cm in diameter remained after the healing of the lesion

The patient's blood pressure was 142 systolic and 82 diastolic His mother had a breast removed because of cancer and died two years later of a heart attack His father died of heart trouble at the age of 85

The serologic reaction of the blood for syphilis was negative on Sept 25, 1944 The urine was normal The blood sugar content was 109 mg and the urea nitrogen content 11 mg per hundred cubic centimeters of blood A complete blood count revealed hemoglobin, 75 per cent, erythrocytes, 4,290,000, and leukocytes, 4,700, with 64 per cent neutrophils, 26 per cent lymphocytes, 8 per cent monocytes and 2 per cent eosinophils

The report on the biopsy specimen was as follows The epidermis was normal, and the corium was almost entirely occupied by the formed bundles of fibrous tissue The patterning of these was unlike that of normal collagenous tissue in that the bundles were longer and straighter, although they still interlaced The nuclei within the bundles were numerous and of mature type There was not the slightest evidence of sarcomatous change The diagnosis was dermatofibroma

The patient was given a total of 1,600 r of roentgen rays from Oct 26 to Nov 13, 1944 (200 r three times a week) With this therapy the patient improved about 40 per cent

**Avitaminosis, Neurogenic Dermatitis** Presented by DR SIGMUND A GRFINBAUM and DR LOUIS GOIDSTFEN

S C, a white man aged 69, shows on the upper and lower extremities an eczematoid type of dermatitis with lichenification, scaliness, excoriation, oozing, crusting and some degree of follicular involvement The entire skin is senile, ichthyotic and somewhat yellowish The pruritus is intense In the inguinal regions there is pronounced adenopathy Dermatitis involving the upper and lower extremities started in July 1942 after the patient had been cutting weeds in the garden He immediately consulted a physician, and whatever the latter prescribed made the eruption worse Thereupon the patient was referred to a clinic, where he was treated for ten months before coming here The patient's past history reveals an insufficient diet, alcoholic habits and an appendectomy He was studied in the medical, gastrointestinal, proctologic, urologic, neurologic, dental and allergic clinics for the cause of his dermatitis He has had roentgenographic examinations of the chest and gastrointestinal tract Nothing unusual was found, except carious teeth, which were extracted He showed positive intradermal reactions to egg white, tomatoes, grapefruit, oats, egg yolk, malt, oranges, spinach, lettuce, wheat, pork, apples and tea Gastric analysis showed achlorhydria

Biopsy of a lymph node from the left inguinal region showed chronic nonsuppurative lymphadenitis

A biopsy specimen of skin was reported on as follows "In a general, broad way the reaction was diffuse dermatitis with major changes in both the epidermis and the corium. The former was highly acanthotic and moderately hyperkeratotic. The acanthosis took the form exhibited in mycosis fungoides, parapsoriasis and atopic dermatitis, the interpapillary pegs being more highly developed in the subpapillary region and extending rather notably into the corium, even as far as the level of the sweat glands. Indeed, at one place rather broad tracts followed the peripheries of the blood vessels in such a way as to form a special aggregation of inflammatory infiltrate. The cells concerned were outstandingly plasma cells, although there were places where the lymphocytes were richly intermixed. Polymorphonuclear leukocytes were scarce, and edema was only moderate. There was not any clearcut evidence of focalization, such as occurs in the specific infectious granulomas. The walls of the blood vessels appeared to be normal. With the dominance of the plasma cells and the absence of polymorphonuclear leukocytes, both *mycosis fungoides* and *atopic dermatitis* appeared to be excluded in diagnosis. Too, there should have been more edema and at least some semblance of eosinophilic leukocytes for atopic dermatitis. In short, only the picture of a nonspecific subacute dermatitis appeared. Frankly, I should favor parapsoriasis if there were fewer of the plasma cells and the infiltration were not so deep. As to avitaminosis (presumably A), it was conceivable that this histologic picture is compatible with that disease, but so far as I know, there is no diagnostic picture of that disease."

The urine was normal, except for a trace of albumin. The hemogram showed a mild hypochromic anemia. The serologic reaction of the blood for syphilis was negative. Chemical examination of the blood showed 97 mg of sugar, 588 mg of chlorides, 120 mg of cholesterol, 75 mg of cholesterol esters and 14 mg of urea nitrogen per hundred cubic centimeters of blood serum. The total protein content of the blood was 8.16 Gm, albumin, 4.25 Gm per cent, and globulin, 3.64 Gm per hundred cubic centimeters. The albumin-globulin ratio was 1.12. The result of the van den Bergh test, direct, was negative, indirect, less than 0.2 mg per hundred cubic centimeters.

Treatment consisted of the administration of 150,000 units of vitamin A once a day, with brewers' yeast and injections of crude liver extract and the application of antipruritic remedies. The results were a gain in weight and an improvement in the dermatitis.

#### DISCUSSION

DR LOUIS GOLDSTIN. I know one should hesitate to make a diagnosis of avitaminosis, because it, like focal infection years ago, is being blamed for almost everything. In this case, however, the man looked a great deal worse when first seen than he appears to be now. In addition to the severe dermatitis he also had a pronounced pustular folliculitis and generalized adenopathy. He was cachectic and emaciated and did not respond to treatment. He was studied thoroughly by the internists for possible carcinoma, but no signs were found. Now, here is a man who does not respond to treatment and is emaciated, whose diet has been insufficient and who has been an alcoholic addict. I thought, therefore, of the possibility of avitaminosis A. The fact is that as soon as he was given vitamin A he started to improve greatly, physically as well as dermatologically.

#### A Case for Diagnosis (Lichen Scrofulosus, Vitamin A Deficiency?)

Presented by DR CARROLL S WRIGHT

E. F., a 12 year old boy, presents scattered groups of acuminate pinhead-sized papules, of three months' duration, chiefly on the flexor surfaces of the extremities. The reaction to tuberculin was positive.

The patient has received 100,000 units of vitamin A daily by mouth for three weeks and one intramuscular injection of 50,000 units of vitamin A two weeks ago

## DISCUSSION

DR SIGMUND S GREENBAUM This boy had been receiving 100,000 units of vitamin A three times a day for a month until about two weeks ago, without great improvement

DR CARMEN C THOMAS He somewhat resembles a boy I presented at the last meeting who did not show improvement until about two months after treatment and whose lesions then almost entirely vanished

DR HERMAN BEERMAN Has any one seen lichen trichophyticus without a kerion? That is another possibility that should be considered

DR SIGMUND S GREENBAUM I examined the scales from one of these patches, and they were negative for fungi

DR FRED D WEIDMAN In cases of lichen trichophyticus of Jadassohn, the scrapings should not be made in the usual way Pains should be taken to pull out some of the hairs I neglected to do that I made two or three examinations in such a case and missed the fungi in the first two, then, fortunately, some of the hairs were pulled out accidentally, and the fungus was found in the hair shaft I doubt that this is a case of lichen trichophyticus, there is not enough inflammation

### Urticaria Pigmentosa Presented by DR CARMEN C THOMAS

J E M, a white boy aged 11 months, presents widely disseminated yellowish papules distributed on the trunk, arms and thighs and especially numerous on the back Some lesions are macular All become elevated and red on slight pressure or friction The disease had its onset in April 1944 and within a few days became generalized and has remained so It is not particularly pruritic The child is a blond blue-eyed adopted baby of English and Irish parentage

The patient has been given dicalcium phosphate with viosterol in oil, 7½ grains (0.48 Gm) three times a day, before meals

## DISCUSSION

DR CARROLL S WRIGHT Was any parathyroid injection U S P tried in this case or has any one tried it in any other case? It seems to work well in the treatment of lichen urticatus

DR H HARRIS PERLMAN I have used parathyroid injection in cases of lichen urticatus, following the teaching of Cornbleet It has been my experience that the lesions clear rapidly with this therapy, plus good-sized doses of calcium by mouth This case, however, is not one of lichen urticatus

### A Case for Diagnosis Presented by COMMANDER H E TWining (MC), USNR

E W, a white woman aged 43, presents sharply defined bilateral symmetric erythema and induration with yellowish brown pigmentation of the anterior aspect of the lower part of both legs The eruption began fourteen years ago Six months ago ulcers developed on both legs and have gradually become larger The physical examination otherwise revealed nothing relevant

The serologic reaction of the blood for syphilis was negative A complete blood count, results of urinalysis and blood sugar test, a roentgenogram of the chest and the basal metabolic rate were all within normal limits

The patient has been given sulfonamide ointments, penicillin locally, red blood cell paste, Unna boots, wet dressings and vitamin A and D ointments without effect

## DISCUSSION

DR D M SIDLICK The fact that impressed me about this case is the presence of healthy granulations forming the base of these ulcers. Apparently it is an attempt on the part of nature to promote healing, but some one or something is preventing it. It is my belief that this is a case of dermatitis factitia. A plastic covering would accomplish a good result.

DR THOMAS BUTTERWORTH, Reading, Pa. These lesions had a definite violaceous border, and the upper part of them had a yellowish cast with telangiectasis. I grant that the cellophane sheen is absent, but I consider that it is a case of necrobiosis lipoidica diabetorum and should be studied from that angle.

COMMANDER H E TWINING (MC), USNR. In all probability most of the members have seen this patient at previous meetings. She is a patient of Dr Ludy's, who treated her for fourteen years. I feel sure that dermatitis factitia can be absolutely ruled out. The upper border of these lesions is not superficial but deep, and the lesions have progressed from a small erythematous area low on the leg up to the knee. Two or three diagnoses have been suggested. She has worn an occlusion boot for a considerable time without improvement. Ulceration started to develop about a year ago. She was at that time decidedly anemic. It was found that she had a uterine tumor, which was removed, but I do not know the diagnosis. She received five blood transfusions, and shortly thereafter the ulcers healed. About six months ago they began to break down again, and, in spite of all therapy, it has been impossible to stop their progress. Dr Weidman saw the biopsy specimen and suggested a diagnosis of lupoid leprosy or possibly a true tuberculosis. He said that there was a definite necrobiosis, but he could not make a diagnosis of necrobiosis lipoidica diabetorum, which I think was Dr Ludy's diagnosis.

DR D M SIDLICK. May I call attention to the fact that the lesions of dermatitis factitia need not be superficial? I recall the case of a woman who had a lesion extending down to the femur, which had existed over a period of years and which was self produced.

DR J M SCHILDKRAUT, Trenton, N J. I think varicose ulcers should be considered in this case, because if one feels the limb one can palpate thrombosed veins. Furthermore, the skin is hidebound, as it sometimes is on legs having varicose veins.

DR SIGMUND S GREENBAUM. A biopsy specimen taken from the upper part of the lesion, not from the ulcerated area but from an area where the skin is rather firm, might be of interest. I believe with Dr Sidlick that these ulcers are of external origin.

DR FRED D WEIDMAN. My first impression, too, was that this lesion was factitial, but Dr Twining and I threshed that out. As everybody, I think, saw tonight, there is a brown wooden brawny infiltration in the peripheral parts of these ulcers, and there is one place where this infiltration can be felt to be separated from the ulcerated parts, that is, it is a more or less satellite part of the ulcerated lesions, a place where ulceration has not yet occurred. I feel sure that the origin of this lesion is deep in the skin, perhaps also in the subcutaneous fat. I will reexamine those sections now that I have seen the patient, but, as I recall it, my thought was leprosy, and I used a stain but did not find any lepra bacilli. Lesions of this kind are known in the lizarine form of leprosy. They do not look like those of leprosy but really are even worse, with a great deal of crusting. In view of the epithelioid reaction that occurred, I am sure the disease is not of exogenous origin. It is, rather, of hematogenous origin, and I think that it is probably some form of tuberculosis. It is not definitely a sarcoid, but I think that it is somewhere in that category—not exactly a frank tuberculosis but some paratuberculous eruption.

COMMANDER H E TWINING (MC), USNR. I might add that this biopsy specimen was taken from a lesion, possibly the size of a quarter, about six weeks

ago, which was altogether isolated from the main area and from what was considered a new advancement of the disease

**Erythema Exudativum Multiforme** Presented by DR BERNARD L KAHN

E B, a white woman aged 38, moderately obese, temperamentally nervous and highstrung, presents bright red deep-seated nodules over the outer portion of the left wrist. There is a similar lesion over the flexor surface of the right wrist. These lesions started about five weeks ago. They are extremely painful, especially during changes of the weather. As the older lesions fade, new ones appear at the margins. The disease dates back to the fall of 1939, when there appeared over the left wrist and the left big toe bright red deep-seated nodules which grew rapidly larger and became elevated. Other lesions appeared on the left thigh. The lesions are painful. Old lesions would disappear and new ones appear in adjoining areas. The eruption continued to June 12, 1941, when the patient was admitted to the hospital for study.

The patient's mother is living and well, but her father died of cancer of the liver. She has three brothers living and well. One brother died of influenza. She has no sisters. There is no history in the family of cardiac, renal or metabolic disease or tuberculosis. Her father had asthma and her mother climacteric depression. The patient had measles and frequent attacks of grip. Her tonsils and adenoids were removed in 1922. She had an appendectomy in 1929. She has had pains in the joints off and on for the past few years.

The urine was normal. A complete blood count revealed hemoglobin, 78 per cent, erythrocytes, 4,490,000, leukocytes, 6,400, with 66 per cent neutrophils, 1 per cent eosinophils, 6 per cent monocytes and 27 per cent lymphocytes. The heart and lungs are practically normal.

The patient has been given cold compresses, rest and sodium salicylate internally.

DISCUSSION

DR FRED D WEIDMAN I agree that these lesions are of the erythema multiforme type, and I should be inclined to add the word hemorrhagic, which speaks for the intensity of the lesion. The interest, of course, centers around what the cause of such an expression might be. I suggest that inquiries be made as to the possibility of iodides and bromides having been used.

DR MEYER L NIEDELMAN This woman gives a history of taking compound effervescent powders every now and then for headache, and I think that inquiry should be made in that direction.

DR BERNARD L KAHN The interesting part about this case is that when the lesions appeared, in 1939, they were typical erythema multiforme lesions. At that time I questioned the patient thoroughly, and there was no history of her having taken bromides at any time, only Seidlitz powders for headaches. The lesions persisted for almost two years, until 1941, when I had her admitted to the hospital because they were severe and the associated pain was almost unbearable. With rest and salicylates the lesions disappeared after a week. They reappeared again just six weeks ago.

DR HERBERT J SMITH I think that Dr Niedelman referred to Bromo-Seltzer and not compound effervescent powders. The latter is a cathartic preparation, while the other is a proprietary remedy for headache containing acetanilid and sodium bromide.

DR FRED D WEIDMAN This is an extremely interesting case, in view of the pain. I think that all those present were struck by that item. Inasmuch as it is so unusual, one might go off on another tangent and examine for foci of infection. I think that every one recalls Osler's work on erythema multiforme and how, of all the visceral lesions that were important, he decided that disease of the gallbladder was the most important. This woman is not the type likely to have disease of the gallbladder, but I think that the possibility of this diagnosis should be looked into.

**A Case for Diagnosis Presented by Dr J V KLAUDER**

D C, a white man aged 32, when first seen, in June 1944, presented flat-topped yellow papules about 0.5 to 1 cm wide scattered over the face, the sides of the chest and the back and a few in each axilla. There were congestive remains and scars of former lesions destroyed with an electric needle by a physician prior to the time I first saw him. The duration was seven months. The lesions were firm and definitely yellowish. The patient has always been in good health. He is overweight and says that he never had disease of the gallbladder or liver.

The Wassermann reaction of the blood for syphilis was negative. There was no sugar in the urine. The cholesterol level of the blood was 310 mg per hundred cubic centimeters of serum.

Biopsy by Dr Fred Weidman disclosed that the epidermis might be regarded as normal, except for atrophy immediately overlying the lesion of the corium. The latter is partly a superficial nodule which produces a slight elevation of the cutaneous surface and partly a localized small mass immediately below it but extending quite to the bottom of the section. It is highly probable that these two portions were continuous at some other level of the lesion.

The chief processes were not distinctive in themselves. Most of the lesions consisted of collagenous bundles which were swollen and edematous, together with a scanty infiltration of inflammatory cells. These were distributed diffusely. Most of them were lymphocytes, but fibroblasts occurred in almost equal numbers. The latter were largely degenerated, as indicated by their pyknotic nuclei. Polymorphonuclear leukocytes were conspicuous by their absence. The most noticeable feature of the section, but one which I regard as having minor significance, was the presence of fairly numerous giant cells. These were distributed scatteringly. Most of them had foamy cytoplasm and at first sight suggested giant cells. Close study demonstrated, however, that the foaminess could be the result of edema, inasmuch as the cytoplasm was traversed by fibrillae instead of being stippled, as in the case of lipid deposits.

I feel that the most significant pathologic change concerned the blood vessels and that this eruption was due to a hematogenous toxemia of some kind. The walls of some of the deeper vessels were so highly edematous and swollen that the lumen was almost occluded, and throughout the section lining endothelial cells of blood vessels were swollen and sometimes hyperplastic. It appeared, even, that blood had escaped from some of the superficial vessels, as indicated by the presence of fine grains of pigment diffused in the tissues and to a less extent within some of the foam cells. I cannot indicate the precise dermatologic diagnosis. I can only place it in the category of toxic diseases which result in fixed tissue reactions such as take place in cases of rheumatism and gout. It is not xanthoma in the ordinary sense, and in fact I doubt that fat of the usual type would be demonstrated. Inquiries should be made into possible hematogenous factors. Secondary xanthomatous changes have been known to occur in scars and other inflammatory infiltrates.

**DISCUSSION**

DR J V KLAUDER: There has been improvement following a fat-free diet.

DR FRED D WEIDMAN: All are agreed that this is a spectacular condition. I was struck by the translucence of the lesions, they are not inflammatory nor is there an inflammatory areola around them, and I should say that the disease resembles milium lupoid. The sections dispose effectually of the diagnosis of xanthoma, at least in the lesion examined microscopically. That was a small lesion. The giant cells are of the Touton type, such as one sees in xanthomas, and I am wondering what one of the larger lesions would show. I still doubt that xanthoma would appear. I believe that the pallid centers are the result of necrosis and that on histologic section larger lesions would show a central focus of necrosis. On reexamining the section of the small lesion tonight, I can understand how a tuberculoid architecture might be found in the larger lesions.



As the case stands, I believe it falls in the category of the tuberculids and possibly a miliary lupoid of Boeck

**A Case for Diagnosis (Eosinophilic Granuloma?)** Presented by DR J V KLAUDER and DR FRFD D WEIDMAN

P R H, a white man aged 50, about January 1944 had a lesion on the back. It was treated by a roentgenologist with roentgen rays, causing it to disappear. The roentgenologist informed us that it was elevated and of ovoid shape and about 2 by 4 cm. It was firm and had a central ulceration. In May another lesion appeared on the left leg. The roentgenologist who treated the one on the back administered five treatments of 1,000 r filtered through 0.1 cm of aluminum. As a result of this treatment the lesion considerably improved.

When the patient was first seen, in October, he presented a mass that filled the concha, concealing the entrance of the external auditory canal. It had a central ulceration, the surface of which was covered with a yellowish membrane, and bled easily. A part of the tumor was on the anthelix. This portion was a plaque with a smooth nonulcerated surface and another portion extended onto the crus helix. These lesions were elevated, varying from 2 to 4 cm, firm to the touch and infiltrated. As a result of wet dressings of an antiseptic solution, the ulcerated portion partly healed and bleeding became less pronounced. Within the past two weeks the mass has become somewhat larger and more infiltrated. The patient complains of pain in the ear radiating to the throat and down the neck. The patient has always been in good health. He has never traveled outside the United States and has not been away from the vicinity of Philadelphia for some years. There is no history of syphilis.

The Wassermann reaction of the blood for syphilis was negative. There is no enlargement of the lymph nodes. Laboratory studies showed a red blood cell count of 4,730,000, 74 per cent of hemoglobin, and 16,250 leukocytes, with 70 per cent polymorphonuclear leukocytes, 10 per cent small lymphocytes, 9 per cent large lymphocytes, 2 per cent monocytes, 5 per cent transitional cells and 4 per cent eosinophils. The Schilling index showed metamyelocytes, 0, stab cells, 11 per cent, and segmented forms, 59 per cent. The multiple index was 3.0, a relatively normal shift.

There was no improvement after three intramuscular injections of bismuth subsalicylate and the oral administration of potassium iodide in doses ranging up to 30 grains (2 Gm) three times daily.

Histologic examination disclosed that the epidermis appeared over the greater part of the section but that at one end it was ulcerated. It was acanthotic, highly edematous and variously infiltrated with polymorphonuclear leukocytes. At the center of the section the interpapillary pegs were elongated and most bizarre in shape and extended as snags quite to the middle of the corium. In our opinion this is an expression of pseudoepitheliomatous hyperplasia and not cancer. In the first place, even in the deepest locations, the cells did not have the large richly chromatinized nuclei—indeed they were pale—and, in the second place, the ulceration was associated with an intense leukocytic infiltration round about. Incidentally, nests of leukocytes frequently occurred within the epithelial downgrowths. Perhaps it is also of significance against the diagnosis of cancer that the epidermis at the edge of the ulcer did not show proliferative tendencies as much as that part which lay at the other end of the section.

The corium was solidly occupied by inflammatory cellular infiltrate, excepting an edematous zone which lay immediately below the epidermis, and even here some straggling cells sometimes appeared. In the deeper parts of the corium it was not possible to identify the slightest trace of collagenous tissue, so dense was the infiltrate. This dense infiltrate had a delicate fibrous framework which was denser in some places and so loose in others as to resemble lattice fibers. Everywhere blood vessels were extremely numerous and thin walled and sometimes associated with small hemorrhages. The cells concerned varied in pro-

portions from place to place. In one place lymphocytes predominated and in others polymorphonuclear leukocytes. Indeed, at some places the polymorphonuclear leukocytes were so sharply focalized as to constitute miliary abscesses. Eosinophilic polymorphonuclear leukocytes dominated the scene in every part of the section.

An additional type of cell was difficult to identify but impressed us as being a monocyte and approached closely the Sternberg-Reed cell. It was scatteringly distributed, never in groups, and this was one reason why we dismissed it as a possible cancer cell which was infiltrating from above. The cytoplasm was clear and sometimes invisible. The cell membrane could never be seen. The nucleus was rounded and large, and a few examples could be discovered which were indented. A great many of them were in mitosis. These nuclei, like the epithelial ones higher up, were poor in chromatin or even poorer. They appeared to be edematous. Micro-organisms were searched for, particularly within the miliary abscesses, but none were found.

The epithelioid cell hyperplasia which characterizes leishmaniasis was not exhibited. There are two diagnostic possibilities. The first one is a squamous cell epithelioma which has been modified by roentgen rays or some other circumstance so that the nuclear chromatin has not been formed. The patterning of the infiltrating cells was altogether good for cancer, but after that there was nothing to recommend that diagnosis. We have already stated the features which were the more in favor of the epidermal changes representing pseudoepitheliomatous hyperplasia. The extreme density and eosinophilia observed in the granulomatous infiltrate we have never seen approached, even in an epithelioma. The second alternative diagnosis is eosinophilic granuloma. From published descriptions, this case conforms with cases of that disease. If it is such, we would view the process as one in which the reticuloendothelial cells were involved in addition to the exudation of the eosinophils. A third alternative, namely, Hodgkin's disease of the skin, can be disposed of in view of the mitotic figures, the absence of any tendencies whatsoever toward fibrosis and to a lesser extent the almost unbelievable numbers of eosinophilic leukocytes.

At this stage in the studies we are unwilling to make any diagnosis with the data at hand. Although we doubt it, there is still the possibility that the disease is cancer, the atypicalness having to be explained on the basis of roentgen radiation therapy together with some systemic peculiarity of the patient which leads to the eosinophilia.

#### DISCUSSION

DR J. V. KLAUDER: It may be pertinent to discuss briefly eosinophilic granuloma.

DR FRED D. WEIDMAN: There is a tremendous mass back of the ear, extending down into the skull, and it seems to me that it has originated there and has extended up to the ear more or less accidentally. That is, this is a tremendously deep-seated lesion. It seemed to me that this lesion was the size of a golf ball, it is not a superficial thing. From the clinical appearance it looks to me as if it had a deeper origin and as if it may be in the bone. In regard to the histologic examination, the question of granuloma arose at once, and there is a remarkable infiltration of epithelial cells. I took a section to Dr Ehrlich, and he thought it was cancer. There are many mitotic figures. But after seeing the lesion tonight and noting how deep it is, I feel that it is not fundamentally cancer. The infiltrating cells do not extend down to the bottom of the section, they do not extend near the center of that really large lesion, and I am inclined to view that hyperplasia as a pseudoepitheliomatous hyperplasia. As an outcome of this consultation with Dr Ehrlich yesterday, I stained some frozen sections for fat and found, as he had suspected, that there was fat in the lesions, mostly in the epidermis but also in the monocytes farther down, and no doubt those monocytes are the structures which gave rise to the suspicion that the disease was related to Hodgkin's disease of the skin. The term "eosinophilic

granuloma" is used in two senses one is in respect to the syphilid of Katz, the other, that which the general pathologist knows as an eosinophilic granuloma, which is a lesion of the bone and which usually occurs in very young people, much younger than this patient. Nevertheless, after observing how deep the extension of this lesion is, I wonder whether this may not be the eosinophilic granuloma of the general pathologist, that is, an osseous tumor. That is my conclusion, after seeing the patient tonight. The histologic picture is highly conflicting. I have never seen such enormous numbers of eosinophils, even in Hodgkin's disease of the skin, and this very clear type of monocyte, and I did find some that had two or three nuclei, like the Sternberg-Reed cells. But this cannot be Hodgkin's disease of the skin because there is not the fibrosis that should be present in that disease. I think that Dr. Klauder's description fits the eosinophilic granuloma which the French have described, but I do not believe that they necessarily have evaluated the pathogenesis of the disease, that is, of the syphilid of Katz. I think that the epithelial changes are not neoplasms in that disease. The French speak of it as true carcinoma, and they try to explain it as a cancer that is affecting both epithelial and connective tissue, the connective tissue being the Hodgkin-like feature. I think that it should be regarded as an eosinophilic granuloma originating in the bones, and I think that a roentgenogram should be taken to see whether the bones are involved.

DR. WILLIAM EHRLICH (by invitation). From all that I have heard, I think that there can be little doubt that this lesion is an eosinophilic granuloma, though none of us have ever seen one. I do not think that it could be Hodgkin's disease of the skin, not only from the histologic picture, as Dr. Weidman has pointed out, but also from the systemic involvement. In Hodgkin's disease of the skin there would be involvement of the lymph nodes of other portions of the body, but in this case the disease seems to be a localized affair. Consequently, I do not think that it has anything to do with Hodgkin's disease of the skin. It is probably eosinophilic granuloma.

## Book Reviews

**Studies in Biophysics The Critical Temperature of Serum (56°)** By Lecomte du Nouy Cloth, price \$3 50 Pp 185, with 89 illustrations New York Reinhold Publishing Corporation, 1945

This book is the recording of a series of biophysical experiments with human blood serum. The pattern of study throughout is a fixed one, called by the author 'kinematic,' as contrasted with "static." By "kinematic" the author means that the choice is made to measure biologic characteristics by securing many records on a single sample revealing the influence on those measurements of a series of different physical influences.

The recorded studies are highly technical and in the field of dermatology could be of some interest only to a serologist.

## News and Comment

### DEATHS

Dr. Henry G. Munson died on April 9, 1946, in the Presbyterian Hospital in Philadelphia.

Dr. Girsch D. Astrachan died in New York on April 30, 1946.

Dr. Robert C. Jameson died in Detroit on April 17, 1946.

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## SYMPOSIUM ON DIAGNOSIS AND TREATMENT OF CUTANEOUS CANCER

### CUTANEOUS CANCER FROM THE STANDPOINT OF THE DERMATOLOGIST

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**T**HE subject cutaneous cancer is to be discussed from various points of view, particularly with regard to modes of treatment. In the limited time at my disposal, I felt it was probably best to discuss only the various types of basal cell and squamous cell cancer.

Basal cell epithelioma is found most frequently on the face, 95 per cent of the lesions occurring above the angle of the mouth, particularly about the nose and eyes. With rare exceptions, this type of cancer does not metastasize, hence it may, on the whole, be looked on as a local disease in the majority of cases. It grows slowly, some lesions taking years to attain a diameter of 1 or 2 cm. Many types of basal cell epithelioma respond to treatment more readily than do ordinary warts. Because of these facts, namely the location of the cancer on the face, the relative ease of treatment and in most instances the lack of danger of the process itself, basal cell epithelioma must be looked on as a disease of mild grade malignancy and its local destruction should be carried out with two major ideas in mind: first, a complete destruction of the lesion itself and, second, and almost as important, destruction of the lesion with a minimum of damage to the surrounding tissues, so that an excellent cosmetic result occurs. Another consideration is that the method of treatment adopted should be such that no future danger to that area of skin will arise as a result of the treatment. It therefore becomes imperative for one to weigh and select each case carefully, taking into consideration the age of the patient, the location of the lesion and its proximity to bone, cartilage, eyeballs and other parts of the body.

This paper is the first in a "Symposium on Diagnosis and Treatment of Cutaneous Cancer," held at the New York Academy of Medicine, Section of Dermatology and Syphilis, on April 4, 1944.

Basal cell epitheliomas occur in many different patterns or types, and these vary materially in response to the different types of therapy. For example, for convenience, both in diagnosis and in treatment, I have classified the basal cell epitheliomas into the following types

- 1 Rodent ulcer, or hard pearly bordered lesion
- 2 Morphea-like type
- 3 Soft nodular type
- 4 Pigmented type
- 5 Superficial cicatrizing type
- 6 Cystic type
- 7 Infiltrating or invasive type
- 8 Multiple basal cell epithelioma

Every one is familiar with the various lesions of the rodent ulcer type, of which some are relatively soft and others have a hard, rolled, almost cartilaginous-like border. The central ulceration not infrequently may be covered with a crust, which should always be removed both to assist in the diagnosis and to facilitate treatment. This variety of basal cell lesion usually responds well to radiation of all types—by that I mean various types of roentgen rays either filtered or unfiltered, low voltage or contact, etc., and radium. It should be a cardinal rule, however, that with whatever type of treatment is selected for a given lesion the lesion should be destroyed in one treatment. While I appreciate the fact that this quick destruction cannot invariably be accomplished, I make it my aim to destroy at least 95 per cent of all basal cell lesions at the time of the first treatment. This means that one must carefully weigh the type of treatment to be used. If roentgen rays are selected and the dose to be used for a given patient to achieve a cure in one treatment seems to be excessive and liable to give rise to so much damage of the skin that the later development of a squamous cell epithelioma may be expected, then that method of treatment is, in my opinion, not suitable. On the other hand, the lesion may not be ideally located for surgical excision. Furthermore, surgical excision and repair may necessitate repeated operation with hospitalization. This should not generally be necessary in the treatment of the usual basal cell lesion.

The dermatologist has, for many years, combined the several types of destruction of such lesions because the cosmetic results achieved in this way are far superior to those achieved by only one method of attack. For example, if the rodent ulcer has an unusually hard and deep rolled pearly border and base, it is a simple matter for one to anesthetize the lesion with procaine hydrochloride and desiccate the hard portion of the lesion. A curet is then employed to remove the desiccated tissue, and by experience one can easily determine when all the cancer tissue has been removed. The lesion is then ready for a dose of roentgen rays or radium, but with this combined method a large dose is not necessary and as a result no sequelae of unpleasant radiation need be

expected. An excellent cosmetic result is achieved, and the patient is cured with little or no deformity. This procedure is particularly suitable for basal cell lesions located on or about the eyelids or the corners of the eyes and on or about the ears at points where cartilage may be destroyed by large doses of radiation, and the same situation of course will apply to lesions of the nose.

The morphea-like basal cell lesion is one that is not usually radiosensitive, and for this reason I believe that lesions of this type are best treated by either surgical excision or excision with the electric knife. As these lesions are flat hard areas with little elevation but with considerable depth and a shiny glazed surface, the patient may permit them to reach considerable size before consulting his physician. As a result, if the lesion is surgically excised, considerable plastic repair generally must be done, and if a surgeon tries to remove as little tissue as possible, fearing that closure will be difficult, a recurrence of the lesion may be expected. For this reason, I have frequently found it advisable to remove these lesions with the electric cutting current, allowing the area to fill in with granulation tissue, and if the resultant scar is not satisfactory it may be removed at a later date for cosmetic purposes. Meanwhile, the patient can be kept under observation to be sure that the cancer has been completely destroyed. While this method might require a second operation if the cosmetic result were not satisfactory, the situation would be no different than if the growth were removed surgically and several plastic repairs made.

The soft nodular type of lesion is radiosensitive and can almost invariably be destroyed in one treatment with a moderate dose of the roentgen rays or radium. The pigmented variety also is usually radiosensitive, or if not it can easily be destroyed by the combined treatment described for the rodent ulcer type.

The superficial cicatrizing type of lesion is seen most commonly on the trunk or the extremities. While this type is said to be radioresistant, it has responded to relatively small doses of radiation in my experience and certainly can easily be destroyed by a combination of desiccation, curettement and radiation.

Lesions of the cystic type are frequently deep seated and when occurring about the eyelids may be hard to destroy by radiation alone. Here again a combination treatment is ideal.

The infiltrating or invasive type of growth, especially if extensive, can frequently be cured by radiation, but if one does not succeed in doing this after giving one or two doses of radiation then I believe that the lesion should be completely excised by the electric cutting current or by surgical intervention.

Multiple basal cell epitheliomas occur mainly on the trunk but they may appear also on the face. They do not represent a special type

but are a variety of one or more of the types previously mentioned and must be treated accordingly

While it has always been the argument of the surgeon that cancer should be removed radically by some cleancut method, such criticism can no longer be leveled at the present day technic of adequate desiccation and curettement, followed by a destructive radiation. As stated earlier, this method is superior to any other in properly selected cases. It avoids the disadvantages of surgical treatment with the knife and the overirradiation that is frequently necessary to cure a lesion in a single sitting, and it gives a cosmetic result so good that it is frequently difficult to locate the treated area. The dermatologist who has specialized in this method and whose technic has been perfected by a combination of surgical and radiotherapeutic training is the ideal one to carry out the method.

I shall now discuss briefly squamous cell epitheliomas of the skin. These lesions differ from the basal cell growths in two major respects. First, they develop rapidly. Second, and most important, the removal of the primary lesion represents only a portion of the possible job to be undertaken. For this reason it is my opinion that most dermatologists, unless fitted by special training in work with cancer, generally are not qualified to treat these growths. Most dermatologists, however, restrict themselves to the treatment of basal cell lesions and of those squamous cell lesions and epitheliomas in which it may be reasonably assumed that the disease has not progressed beyond the primary lesion. There is another type of case in which the dermatologist might be called on to treat a cutaneous cancer but because the growth is considered inoperable he, therefore, must use the radiation at his disposal to palliate rather than to cure the disease.

While the majority of the cancers on the face, especially those above the angle of the mouth, are of the basal cell type, at least 95 per cent of those occurring on the extremities are squamous cell ones. I believe it is probable that squamous cell lesions on the face above the angle of the mouth occur in slightly more than 5 per cent of cases and that one does not see basal cell lesions occurring on the extremities in as high as 5 per cent. Squamous cell lesions, therefore, are encountered most frequently on the extremities on the mucous membrane surfaces and as a sequel to other dermatoses. The lesions of the mucous membranes whether located on the lip, buccal mucosa, tongue or genitalia, should not, in my opinion, be handled by the dermatologist. My reason for this statement is that metastasis from such primary sites may occur as early as three or four weeks after the lesion has been discovered by the patient and that what may seem to be an early lesion is actually a late one. There is no doubt that the primary lesion can be destroyed by



the dermatologist as well as by the surgeon or the radiotherapeutist but if the lymph nodes are to be treated by dissection he is generally unqualified

The early squamous cell lesion of the glabrous skin, occurring particularly on some portion of the face, is a lesion that I believe dermatologists are qualified to treat. This is the lesion which is frequently not recognized and yet presents just as typical a clinical appearance as do most of the types of basal cell lesions

#### DESCRIPTION OF THE TYPICAL LESION

The development of the nodule is usually rapid beginning frequently as a papular lesion of pinhead size and reaching a diameter of 1 to 2 cm in from three to six weeks. After this period, the growth is somewhat slower. In patients under 45 to 50 years of age it is more rapid than in older ones. The typical squamous cell epithelioma of the glabrous skin begins first as a small grayish nodule covered with a scale or crust. As it increases in extent and depth, the crest assumes a reddish color and may become ulcerated or verrucous. The tumor which develops is hard, firmly embedded in the skin and yet protuberant. Its raised, bulging border presents a glazed or waxy appearance. The presence of numerous small blood vessels in the border gives the base an acute inflammatory appearance which is characteristic. The upper and outer portion of the border is usually more or less hyperkeratotic, and in the central area an erosion appears. The latter develops into a crater-shaped ulceration which is irregular, fissured and grayish and bleeds easily even on slight irritation. The appearance of the lesion at this stage may easily simulate that of a large infected verruca, sebaceous cyst or a tumor of large molluscum contagiosum. The vascularity of the base of the growth gives the appearance of an infection. On the floor of the central crater there can be seen yellowish gray granules or material simulating the cheesy contents of an infected sebaceous cyst. The latter substance is composed of horny cells and epidermic globules.

Little mention is made of this growth in most of the dermatologic or surgical textbooks. When the lesion has been described, the author has frequently expressed the opinion that metastasis may occur early to the regional lymph nodes. This was Darier's<sup>1</sup> belief, but he also expressed the opinion that generalization to the viscera was rare. In all the patients which I have seen, I have encountered only 1 instance of local metastasis to a regional lymph node, and when this node was excised the patient remained free of further cancer for a

<sup>1</sup> Darier, J. Text-Book of Dermatology, translated from the French by S. Pollitzer, ed 2, Philadelphia, Lea & Febiger, 1920

period of three years, during which I was able to follow him. My interest in this type of lesion dates back over twelve years, and in 1933 Dr Tolmach and I<sup>2</sup> reported on 26 cases of similar lesions and our method of removal.

Briefly, the method of treatment that we suggested consisted of excision with the electric cutting current. At first we felt that it might be advisable to follow such excision with radiation, but, as most of the lesions can be easily excised in toto, there seemed to be no point in following a complete excision by irradiation. Therefore, only when one is uncertain whether the excision is complete need the excision be followed by irradiation. In most of our cases, in all of which the development was early—not over three months—it was not found necessary to either irradiate or excise the nodes.

Little need be said about squamous cell lesions involving cartilage, because I believe that they require surgical excision.

In dealing with lesions on the extremities, particularly on the dorsal surface of the hands, the local lesion may be excised in toto by the dermatologist if the lesion is early and if no metastasis in a node can be palpated. On receipt of the report of the pathologist, should the lesion be of the more malignant type, consultation with the surgeon as to further disposition of the case may be advisable. If the lesion on the extremity is of long standing and if there is no doubt that metastasis has occurred, then certainly the entire management should be turned over to the surgeon.

Squamous cell cancer occurring as a sequel to other dermatoses should be managed much as I have suggested for lesions on the extremities. When the change to cancer is suspected, the lesion is small and metastasis not apparent and the diagnosis still needs microscopic confirmation, it is frequently better for the dermatologist to excise the entire lesion than to perform a diagnostic biopsy. The reason that I prefer this procedure to performing an ordinary punch biopsy is that so frequently with a punch biopsy or excision of a small portion of tissue one does not obtain sufficient material for a conclusive diagnosis or the tissue may be taken from a portion of the lesion not characteristic of the entire mass, hence it might become necessary to perform several biopsies, with the loss of valuable time, before a correct conception of the growth may be obtained. All such difficulties are obviated by excising the entire lesion and examining it in toto.

2 Traub, E. F., and Tolmach, J. A. Squamous Cell Epitheliomata of the Skin of the Face, *New York State J. Med.* **33** 875 (July 15) 1933.

## SUMMARY

- 1 The dermatologist is, in my opinion, best qualified from the standpoint of his diagnostic and therapeutic training to treat basal cell cancer. He is not limited to surgical methods as the surgeon is nor is he limited to radiation therapy only, as is the radiotherapist. He is able to remove and at the same time irradiate basal cell cancer, achieving through office treatment what the surgeon frequently can do only after repeated operations and hospitalization and what the radiotherapist can do only after a loss of time and a dosage that may well pass the limit of advisability.
- 2 He is able to destroy basal cell lesions at one sitting with a cosmetic result that cannot be surpassed.
- 3 The dermatologist is qualified to treat early squamous cell epithelioma of the glabrous skin. He is able to make a diagnosis early and to treat an early squamous cell epithelioma which is superimposed on precancerous dermatoses.

## EARLY DIAGNOSIS OF CANCER OF THE SKIN

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AT THE beginning, cancer of the skin proper must be distinguished from cancer of the mucocutaneous junctions. The dermatologist is often called on to diagnose cancer of the lips, tongue, floor of the mouth and buccal mucosa, cancer of the mammary gland and cancer of the genitals and rectum. He must be familiar with these cancers, and in their diagnosis his opinion is often given much weight, but the time tonight will be devoted to a discussion of cancer of the skin proper, and I will speak for only a few moments on its recognition and diagnosis. It is commonly known that skin of certain types is predisposed to the growth of cancer. There is probably no fact regarding the cause of cancer better established than that habitual exposure to sunlight of a fair sensitive skin and maturity are factors that together favor the development of cutaneous cancer. One third of all cancers of the skin occur on the nose and cancer is common on the rim of the ear. In a category similar to that of farmers' and sailors' skin is the cancer which occurs in xeroderma pigmentosum and in chronic radiodermatitis. Moreover, the likelihood of cancer is augmented if, in addition, there are moles, warts or other so-called precancerous lesions present and also if there is contact, occupationally or otherwise, with arsenic or with pitch, tar, paraffin, lubricating oils or other hydrocarbons containing dibenzanthracene or similar carcinogenic substances.

The early symptoms of basal cell epithelioma should now be considered because this disease is so common. Basal cell epithelioma develops on an inconspicuous slightly erythematous scaly spot, which becomes a little thickened, glistening and waxy. The thickening may be so slight that it is barely perceptible. The waxy color is of glistening semi-translucence or of a pearly appearance. The earliest lesions are like small inverted buttons, slightly elevated above the surface of the skin. Small waxy papules coalesce to form a plaque-like lesion, and at the border of this similar papules fuse and produce an elevated rolled border. The central portion becomes crusted, and when this crust is knocked off or pulled off there is bleeding, another crust forms, and

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this sequence of events continues. In crusted lesions, the waxy color may not be apparent until the crust has been removed. The duration is usually a matter of years, sometimes of only a few months and often of many years.

In addition to the common button type and plaque type basal cell epitheliomas, there are many other clinical types, of which the rodent ulcer is the most important. It is a burrowing, mutilating, destructive growth which occurs mostly about the eyes, the ears or the nose. In these locations, it may cause complete destruction of the orbital contents or of the external ear or nose. It may even cause death through intercurrent disease, such as erysipelas, bronchial pneumonia, sinus thrombosis, epidural abscess or meningitis. The ulceration is deep and punched-out like a gumma. The floor of the ulcer is dirty and the edges are crusted. After the crust has been removed, a rolled waxy border may be discernible. The long duration and the presence of this waxy border may warrant the clinical diagnosis of rodent ulcer, but this must be confirmed by biopsy.

Many other clinical varieties of basal cell epitheliomas are definite entities, but there is not sufficient time to go into the details of all of these. Cancers of the cicatrizing, or scar-forming type all possess the essential characteristics: waxy, glistening appearance, rolled border and a tendency to form crusts and to bleed occasionally. Microscopic study of these lesions reveals many differences between the individual growths, and one feature which is important is the presence in many of these lesions of squamous cell proliferation. Such growths are classified as mixed basosquamous cell epitheliomas. Their importance lies in their clinical resemblance to pure basal cell epitheliomas and their occasional recalcitrance to treatment. Rarely if ever do basal cell epitheliomas metastasize, but sometimes the squamous cell portions of mixed basosquamous growths follow a clinical course like that of squamous cell epithelioma.

The distribution of basal cell epitheliomas is chiefly over the upper portion of the face, above the line drawn from the corner of the mouth to the lobe of the ear, being specially common on the nose, lower eyelid, forehead, cheeks and ears. However, they can occur, and often do, on the chin and less frequently on other parts of the integument. The adenoid type is found chiefly on the forehead or scalp or near the eyes.

Squamous cell epithelioma is sometimes like the waxy growth of basal cell epithelioma, but more often, and more characteristically the squamous cell epithelioma is a warty growth. One must keep in mind the fact that I am speaking of squamous cell epithelioma of the skin

proper and not of squamous cell epithelioma of the mucocutaneous surfaces

On the skin proper, where the lesion is dry, there is much cornification. The horny part of the growth, which gives the wartlike appearance, is due to dyskeratosis, and this horny projection is an inherent part of the tumor. It is thus entirely different from the loosely attached crust of the basal cell epithelioma. Although this horny projection resembles a wart, it differs from a wart in that it arises from an indurated tumor base. If the squamous cell epithelioma is diagnosed in this early, warty stage, the prognosis for treatment is excellent. In the course of time, if the lesion is not treated at this early stage the horny projection is knocked or picked off, with resulting ulceration and eventually induration develops in the underlying tissues and metastasis may occur. The mortality from epithelioma of the skin, however, is low, being under 2 per cent, cancers on the fingers and hands are the most likely to metastasize.

## CUTANEOUS CANCER FROM THE SURGEON'S POINT OF VIEW

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IN the treatment of carcinoma of the skin I feel that cauterization of the lesions alone is not the treatment of choice. Unless it is thoroughly done, the treatment is inaccurate and often ineffectual, and if carried to a depth sufficient to destroy the disease unsightly scarring results. Healing is delayed, the period of dressings may be long, and there is no certainty that the disease has been completely eliminated as there can be no study of sections of the tissue destroyed.

The two main methods of treatment of carcinoma of the skin are irradiation and surgical excision.

In the earlier smaller lesions there are certain locations where irradiation is preferable to surgical treatment because of the difficulty of excising the lesion adequately without causing deformity or without complicated plastic procedures. A sample of such a location is the tip of the nose. There are other locations, such as the external auricle, where irradiation may cause a chondritis that becomes painful and difficult to heal.

Many radiosensitive epitheliomas are eliminated by irradiation without noticeable scarring, those that are radioresistant may be difficult to eliminate by this means. With surgical treatment inasmuch as the majority of epitheliomas occur in the later decades of life, the subcutaneous fat is atrophied and the skin is loose excision in the form of an ellipse with extensive undermining of the skin allows closure to be made more readily in this class of patients and with less resultant scarring than in those in the earlier decades of life. Irradiation sufficient to eliminate the disease may injure underlying tissue and may cause later sclerosis of the skin, pigmentation, telangiectasia, ulceration or even epithelioma. No such complications occur after surgical intervention, and the treatment of these complications should be surgical. Keloids occur but rarely and fine inconspicuous scars usually result from surgical treatment.

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Within recent years improvements in technic in the treatment of these lesions by irradiation have made it possible to eliminate the disease more certainly and with less deformity than in the past. On the other hand, a greater knowledge of plastic procedures for closure is more widespread among surgeons, and less decided deformities result from surgical methods nowadays than formerly.

Information regarding the nature of the lesion cannot be obtained if irradiation alone is used to eradicate the disease. Even if a biopsy previous to irradiation is made, such a biopsy may not always show the complete picture of the malignant process. Possibly the scarring from irradiation may be a more conspicuous deformity than that produced by surgical excision with plastic closure. In small lesions biopsy excision—that is, elimination of the lesion by a sufficiently wide margin to excise it completely—has the advantage of making possible the microscopic study of the lesion, the determination by the pathologist that the lesion was completely excised, and the character of the lesion so that one is able to determine whether metastases may be expected. This is also true of the larger lesions. It is possible, therefore, for the pathologist to advise the surgeon that dissection of regional nodes should be performed. There is an uncertainty about the elimination of the disease by irradiation that is absent with wide excision and careful study of the specimen. The patient's mind can be put at rest with a favorable report from the pathologist.

In each case the first aim of the dermatologist, the radiotherapist and the surgeon should be complete eradication of the lesion at the first treatment. Ineffectual irradiation may cause the cells to become more resistant to subsequent irradiation, and I feel strongly that if the first irradiation is not successful it is better to resort to surgical intervention at once rather than to continue ineffectual irradiation. The greater the amount of irradiation, the more difficult becomes the plastic problem of obtaining healing with primary closure, with free grafts and with pedicle flaps to fill the defect after excision. On the other hand, excision should be sufficiently wide to eliminate the disease at the first attack. In certain instances, if the pathologist finds that the tumor has been cut into and indicates the location on the piece excised, further excision may be made and the disease may be eliminated. This, however, should be infrequent if the surgeon is imbued first with the necessity of taking a wide enough margin of normal tissue to make sure that the excision is well beyond the tumor. His second objective should be that of restoring the part to its normal condition insofar as it is humanly possible. The surgeon who has the various principles and procedures of plastic repair in his armamentarium is a safer operator than the surgeon who lacks this knowledge, as the former can afford to take



wide enough areas to eliminate the disease, because he knows that he can restore the part by one of several methods with comparatively little deformity in most cases. The surgeon without this knowledge tends to cut too close to the tumor for fear that he will not be able to close it without great deformity, and, frequently, insufficient tissue is excised with resultant recurrence.

The pathologist, the dermatologist or radiotherapeutist and the surgeon should know what can be done by each method of treatment, they should meet in the clinic and consult with an impartial point of view to determine which procedure, irradiation or surgical treatment, is indicated from the standpoint of the patient's best interests. In private practice the questionable case should be referred for opinion. It would also be of value to the surgeon and radiotherapeutist to see cases with the dermatologist in order to become familiar with lesions which simulate epitheliomas. It is doubtless true that an expert radiotherapeutist is better than a poor surgeon and a capable surgeon is better than a poor radiotherapeutist.

## TREATMENT OF CUTANEOUS EPITHELIOMA

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**E**PITHELIOMA of the skin may be successfully treated by various means, and no hard and fast rules should be established. The surgeon who is familiar with the advantages and disadvantages of each method has a greater chance of attaining good results than the surgeon whose experience is limited. Obviously this requires a knowledge of the peculiarities of behavior of the various types of cancer and the limitations which the location of the cancer imposes on the treatment chosen.

### ROENTGEN RAY THERAPY OF EPITHELIOMAS OF THE SKIN

*High Voltage Roentgen Rays*—Roentgen rays with a peak kilovoltage of 200 kilovolts or more are seldom used in the treatment of cutaneous cancer, except for deeply infiltrating epitheliomas. It is impossible to sterilize metastatic epidermoid carcinoma in lymph nodes by high voltage roentgen irradiation therapy alone. While this treatment does exercise a restraint on growth to some extent, it should be recognized as a palliative treatment only. For curative attempts high voltage roentgen ray therapy should be supplemented by interstitial irradiation or radical surgical dissection.

*Low Voltage Roentgen Rays*—Roentgen rays with a peak kilovoltage of 100 to 140 kilovolts are of great value in the treatment of cutaneous cancer. A target-skin distance of 30 to 40 cm. is used, either without a filter or with 1 to 2 mm. of aluminum added, depending on the depth dose desired. Thick or deeply infiltrating cancers require an increased depth dose, which is obtained by the use of higher voltage, greater target-skin distance and heavier filters. Superficial cancers need lower voltage, shorter target-skin distance and less filter or no filter at all.

The normal skin surrounding an epithelioma is shielded with lead during roentgen ray treatment. If roentgen rays of low intensity (100 kilovolts) are used, 1 mm. of lead will remove more than 99 per cent

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of the radiation, although half this thickness is usually employed. This sheet lead foil, 0.5 cm in thickness, is easily cut and molded to fit each individual epithelioma, leaving an additional 5 mm or more in width on all sides of the margin of the lesion. The lead protective shield is held in place with adhesive plaster or by contact pressure from various-sized cylinders, which are attached to the open port for the purpose of limiting the field of irradiation. Correction in the roentgen dose at the surface must be made when these shields and cones are used, because only the central portion of the beam is utilized. It is a well known physical law that the smaller the field the less the depth dose obtained, owing largely to a decrease in the scattered tissue radiation.

Low voltage roentgen irradiation requires a greater number of roentgen units to cure an epithelioma of the skin than higher voltage roentgen irradiation. The epitheliomas may be treated by daily fractional doses of 250 to 350 until the total dose approximates 2,500 to 4,000. When epitheliomas of the face are treated, the total dose may be increased by at least 50 per cent. Cancers of the face can readily be treated at a single sitting if no filtration is used.

MacComb has determined the erythema dose for different-sized skin portals when the roentgen rays are generated at 100 kilovolts and 5 milliamperes, giving an intensity of 270 r per minute at 30 cm target-skin distance without filter. The half-value layer of the radiation was 1 mm of aluminum. He found that for skin portals with diameters of 0.5 cm, 1 cm and 2 cm 350 r produced an erythema in 80 per cent of the cases. For fields or portals of 3 and 4.5 cm in diameter, 280 r gave an erythema. This principle was applied to the treatment of a series of 50 patients with epitheliomas of the skin. Not one of the epitheliomas exhibited satisfactory regression when the dose was less than  $12\frac{1}{2}$  threshold erythema doses. On the basis of these results, MacComb constructed a table in which the given doses were considered sufficient for epitheliomas of various diameters.

*Chaoul Contact or Short-Distance Roentgen Therapy* The Chaoul x-ray outfit is limited to a voltage range of 50 to 60 kilovolts. The thin copper filter (0.2 mm) or transmission anode is so placed that the tube operates at contact or 3 to 5 cm target-skin distance. It has applicators of various sizes and shapes to be placed against the epitheliomas. A soft beam is utilized, and these rays are largely absorbed in the superficial tissues, i. e., the cancer. For contact application, the rate of emission is approximately 800 r per minute, for a target-skin distance of 3 cm, it is 88 r per minute, and for a target-skin distance of 5 cm, it is 36 r per minute. Daily fractions of 250 to 400 r units are given, with total doses ranging anywhere from 3,000 r units. Epitheliomas on the face may receive the total dose at a single exposure, for contact application this is seldom more than 3,000 r.

This apparatus has a special usefulness only for the treatment of superficial cancers. Because the depth dose is not great and the major portion of the radiant energy is absorbed by the tumor proper, the deep structures are uninjured and the hazards of late radiation necrosis are considerably lessened. The reaction is sharply localized around the cancer.

*Philips Contact Roentgen Ray Therapy* The indications are the same as those for the Chaoul machine. The inherent filter of the tube and shock-proof shield is the equivalent of only 0.2 mm of aluminum. If additional filtration is necessary, disks of aluminum of 1 or 2.5 mm thick may be inserted over the end of the tube and held in place by attached treatment cones. The diameter of the emergent roentgen ray beam is slightly less than 2 inches (5 cm). The intensity is always at 50 kilovolts constant potential. Two milliamperes is the current employed, although the tube is capable of functioning at 3 milliamperes if the time of treatment is short. The distance of the focus from the target to the protection cap over the end of the tube is 18 mm. Over this end is placed a localizing cone, which increases the target-skin distance to 2 cm. The actual tube is within a long light metal cylinder, which is handled at will by means of an attached grip. The dose administered to epitheliomas of the skin ranges from 3,000 to 8,000 r units, usually in fractions of 400 r units.

*Radium*—At the Memorial Hospital for the Treatment of Cancer and Allied Diseases there are four standard radium applicators in general use, and their different surface areas render them suitable for treating many small cutaneous cancers.

The filtration of these plaques is equivalent to 3 mm of brass, which is the total filtration of the radium or radon capsule usually 0.2 to 0.5 mm of platinum—plus the thickness of the brass case of the plaque. The plaques are applied at a distance of 1 cm, with the exception of the tray, which has a radium-skin distance of 3 cm. Small blocks of balsa wood or Bakelite are used to maintain this distance. The region surrounding the cancer is shielded by heavy lead to protect the normal adjacent tissues.

A cutaneous cancer which is more than 1 cm in thickness or shows deeply infiltrating properties should not be treated with radium at contact or at a radium-skin distance of 1 cm, as it delivers only 30 per cent of the skin dose when the radium plaque is used. The dose at a depth of 1 cm when the radium tray is employed at a 3 cm radium-skin distance is 62 per cent and therefore offers a better method of treatment for the deeper epitheliomas. All epitheliomas which are more than 1 cm in thickness or measure more than 3 cm in diameter should be treated by low voltage (100 kilovolts) roentgen rays.

*Radium Moulage* Whenever contact application of radium is desired over very irregular surfaces, the moulage of a dental modeling compound or wax is a valuable adjunct to radiation therapy. The radium tubes of 0.2 to 0.5 mm of platinum filtration are held in direct contact with the uneven contour of the epithelioma. The dose is computed on the basis of 75 to 100 millicurie hours per square centimeter, with the smaller dose used when the cancer covers a larger area. A dose of 15 millicurie hours per square centimeter applied by contact with a 0.5 mm. platinum-filtered radon tube is equal to 1 threshold erythema dose. Penetration of the radiating beam is very little, and if the cancer is more than 5 mm in thickness either supplementary interstitial irradiation should be employed or the radon or radium tubes should be implanted more deeply into the moulage, to give a greater intervening distance and a correspondingly better depth dosage. Regardless of histologic grading, the dose selected is usually the one capable of sterilizing the most radioresistant epidermoid carcinoma with preservation of the normal tissues. Radium moulages are especially desirable for superficial cancers about the ear, nose and lip.

*Radon Seeds* Radium may be placed in solution (as chlorides), and the radon gas emanating is pumped off by means of a Failla radon apparatus into small capillary tubes having a wall of gold 0.3 mm thick. Gold radon seeds for interstitial irradiation are 4 mm long and usually contain 1.2 to 3 millicuries per seed. They remain permanently in the tumor long after the radon has been completely dissipated.

Gold radon seeds are indicated in the treatment of small recurrent cancers or whenever interstitial radon is desired as an adjunct to contact or short distance radium therapy by moulage or plaque. Their chief value is in the treatment of small cutaneous cancers of the ear, eyelid or face. They should not be inserted too near cartilage or a painful and chronic perichondritis may follow.

*Radon Bulb* Radon in the quantity of 300 to 600 millicuries is collected at intervals and pumped into a tiny glass sphere embedded in a wax cup at the end of a long handle. This glass radon sphere is placed in direct contact with lesions of the skin to give doses varying from 200 to 600 millicurie minutes. This method of employing radium is limited to precancerous lesions, particularly keratoses, and to very small and superficial basal cell epitheliomas, less than 2 mm. in thickness.

#### SURGICAL TREATMENT OF EPITHELIOMAS OF THE SKIN

The procedure of choice for cancers at different locations will be considered later. Since the surgical technic varies with the anatomic location of the tumor, no attempt will be made to discuss this in general.

A few brief comments will suffice to bring out the important points in this method of approach

The line of excision should be carried well beyond the palpable margins of the tumor. Deep incisions should be so directed as to avoid injury to important nerves and blood vessels. If immediate skin grafting or transplanting is planned, a sharp scalpel should be used. No hard and fast rule can be laid down, the location and nature of the cancer determine the operative technic. Endotherm excision, with or without preliminary coagulation of the cancer, may be carried out if immediate skin grafting is not planned. This technic is especially adapted for vascular large recurrent cancers.

Amputation is indicated in the following circumstances (1) when the cancer has invaded so deeply and become so adherent that excision is an impossibility, (2) when the interior of a large articulation, such as the knee or ankle, is extensively laid open, (3) when large areas of bone are exposed, a condition which results in necrosis, (4) when profound and uncontrollable suppuration of the wound is complicated by fever and a dangerous toxemia and (5) when the functional result, even after a presumptive local cure, would be unsatisfactory, the limb becoming an encumbrance.

#### FACTORS INFLUENCING THE CHOICE OF TREATMENT

1 *Location of the Cancer* A cancer in close proximity to bone or cartilage should be treated by surgical intervention, as heavy irradiation may cause a perichondritis, periostitis or osteitis, which may slough and remain painful for many months. This would include epitheliomas located on the dorsum of the hand or foot, anterior tibial region, midline of the back, midsternal region and scalp. On the other hand, surgical excision of epitheliomas involving the eyelids, nose, ear, external auditory meatus and penis may sacrifice organs and tissues which are difficult to restore by plastic reconstruction. Radiation therapy is the method of choice provided the tissues are not involved by cancers too deeply infiltrating and destructive to be amenable to conservative irradiation.

*Eyelids* While irradiation is preferable to surgical excision for epitheliomas of the eyelids, it is important to consider the advantages and disadvantages of the various types of irradiation available. The dangers to the eye from irradiation are two: late cataract and iridocyclitis which may terminate in glaucoma. When low voltage roentgen rays are directed through small cones to the epithelioma and the eyeball is protected by a small lead shield inserted in the conjunctival sac, the lens receives practically none of the dose delivered to the tumor. Thus this becomes the method of choice in this location for these reasons: (1) the general availability of roentgen therapy, (2) the

avoidance of late sequelae, such as cataract, and (3) the difficulty in shielding the eyeball when radium plaques are used

**Nose** The majority of tumors of the nose are of the basal cell type and respond with good results to radiation therapy. Low voltage roentgen ray therapy is preferred, but radium plaques give successful results. It is imperative that the dose be calculated carefully, in order that a perichondritis and chondritis with the possible result of a painful ulcer may be avoided. The actual cautery or endotherm knife is indicated when the cartilage is deeply invaded.

**Ear and Auditory Canal** Radiation therapy is indicated, unless the cartilage is largely destroyed. Low voltage roentgen rays or contact radium therapy by means of a moulage are equally successful. The superficial insertion of gold radon seeds is used for cancers of the external auditory meatus.

**Hands and Feet** The skin over bony prominences is usually poorly nourished, and for this reason irradiation is not indicated. The only possible exception occurs when the epithelioma of the dorsum of a hand or foot is superficial and not of great thickness. Radium plaque treatment or low voltage roentgen therapy administered in fractional daily doses by the Coutard technic is preferable. Cancers of the sole, especially the heel, are usually treated by surgical excision. After irradiation the skin will not tolerate injuries or weight bearing. If muscles, tendons or bone are involved, partial amputation of the hand, foot, finger or toe may be necessary.

**Scalp** Some of the epitheliomas are of the basal cell type, others are squamous cell carcinomas, some of which originate in sebaceous cysts. Although the scalp is highly vascular and should support irradiation well, late radionecrosis or later recurrence often follows radiation therapy. If the epithelioma is at all evasive, wide excision by electrocautery down to the pericranium is the treatment of choice. Involvement of the pericranium calls for sacrifice of this structure and perhaps of the outer plate of the calvarium.

**2 Type and Stage of Cancer**—The basal cell epitheliomas of the skin grow slowly and, because of their long duration, are usually detected early, while they are still superficial and before they have attained great size. Irradiation can be used for the ordinary small ulcerating tumors of this type, with the radium plaque as the method of choice. On the other hand, the basal cell tumors which contain mucin and have a decided adenoid appearance (adenoid cystic epithelioma) are radioresistant.

The factors of fixation and infiltration are more important than the histologic grading in the radiosensitivity of epidermoid carcinoma. This tumor grows more rapidly than the basal cell carcinoma. Spindle cell metaplasia of epidermoid carcinoma increases the radioresistance.

to a degree wherein the cancer will remain viable, even though the normal surrounding tissues will slough from overirradiation

A papillary carcinoma covering extensive areas should be removed in part by surgical endothermy, with irradiation being applied to the base. If the epithelioma occupies a large surface area, fractional roentgen ray therapy is preferred to a massive single dose. If the lesion exceeds 6 cm in diameter, a single treatment of 4,000 r should not be given. Protracted fractionization of the dose is desirable if the cancer is infiltrating deeply.

Irradiation is contraindicated in the presence of fixation, e. g., in squamous cell carcinoma of the dorsum of the hand. Invasion of the bone by contiguity is extremely radioresistant, and surgical excision is indicated. The adenoid cystic type of basal cell carcinoma has a tendency to involve bone.

*3 Treatment of Recurrent Cutaneous Cancers*—When a cancer of the skin recurs after irradiation, as a rule further irradiation is not indicated. There is a loss of the original radiosensitivity, and a larger dose of irradiation would be required. At the same time the normal adjacent tissues are more prone to radiation ulceration. The location of the cancer, the amount of previous irradiation and the histologic type of the cancer must be taken into account before one may arrive at a decision for further treatment by this means. If the recurrence occupies only a small proportion of the original cancer, it may be treated by gold radon seeds or external irradiation with the healed area protected by lead. In the presence of spindle cell metaplasia, surgical excision is imperative.

Cancers recurrent after incomplete excision do not respond to irradiation, as the cells are growing in scar tissue and the tumor is deep in or beneath the skin. In some instances, however, gold radon seeds have been inserted at intervals of 1 cm along the line of incision or into the recurrent tumor if it is palpable.

*4 Selection of Treatment of Cancers of Certain Types and Origins*—The method of choice will be presented for some of the commoner types of cancer with which many surgeons have to deal.

**Bowen's Disease** This tumor should be considered a true carcinoma, and the treatment should be the same as for squamous cell carcinoma.

**Paget's Disease** While this lesion appears on the skin, it is associated with deeper tumors in the ductal system of the breast. For this reason it should be treated as carcinoma of the breast, with amputation.

**Cancer in Acrodermatitis Chronica Atrophicans** Irradiation frequently results in immediate or late ulceration, and wide surgical excision followed by skin grafting is the method of choice.



**Cancer in Xeroderma Pigmentosum** The use of roentgen rays and radium has no place in the treatment of this disease. Excision by knife or endotherm or coagulation by diathermy or cautery should be undertaken.

**Cancer in Lupus Vulgaris and Lupus Erythematosus** In many instances the patients have received previous low voltage roentgen ray therapy for lupus, and the epitheliomas developing later are essentially scar tissue, which may not tolerate a cancericidal dose of irradiation. Wide surgical excision with plastic repair may be necessary.

**Arsenical Cancer** The epitheliomas which develop on these precancerous lesions may be either squamous cell or basal cell in type, slowly growing, somewhat radioresistant and metastasizing late to regional lymph nodes. Because of their superficial nature in the majority of cases, they are usually treated by the application of radium plaques. Low voltage unfiltered and lightly filtered roentgen rays are also suitable for treatment either with the 100 kilovolt machine or with the Chaoul or Philips short distance outfits. When these lesions develop on the palms or soles, they often respond to irradiation but late necrosis may develop. This requires surgical excision, with considerable disability over a long period. The current trend in the treatment of this type of cancer is toward wide and deep surgical excision followed by immediate whole thickness skin grafts.

**Cancer in Chronic Radiation Dermatitis** These cancers are notoriously radioresistant. They are usually squamous cell carcinomas, occasionally exhibiting a spindle cell metaplasia, with a high degree of malignancy. They metastasize relatively early to regional lymph nodes. The proper treatment is either wide surgical excision with immediate application of whole thickness skin grafts or electrocoagulation followed by endotherm excision and secondary skin grafting.

**Cancer in Burn Scars** These cancers are slowly growing radioresistant neoplasms, almost invariably of the squamous cell type. Wide radical excision followed by skin grafting is the treatment of choice.

All scar tissue is intolerant of irradiation, which presents the following difficulties: 1 The squamous cell cancers originating in scars are highly differentiated, adult, radioresistant neoplasms. 2 Owing to insufficient blood supply, the normal process of repair of the tissue reaction following irradiation is weak or absent in the scar bed. 3 The constant infection of these ulcers interferes with successful irradiation. 4 Radionecrosis and sloughing occur quickly and with relatively low doses. When irradiation is unsuccessfully employed, it makes the base of the ulcer more fibrotic than ever and impairs healing. In such an event, the radiation therapy should be followed by wide excision and skin grafting.

**Cancer in Draining Sinuses** Osteomyelitic, tuberculous or operative sinuses of long duration are sources of chronic irritation in which cancers, usually of the squamous cell type, not infrequently develop. The first problem is to eradicate the cause of the sinus if possible, and wide surgical or endotherm excision offers the only hope. In some instances, external and interstitial irradiation have been successful. Although essentially a scar cancer, the growth is usually papillary and somewhat radiosensitive. The divided dose technic rather than massive roentgen ray therapy gives better results. If gold radon seeds are used, they are inserted through the normal surrounding skin. Even after successful radiation, treatment debridement is often necessary.

**5 Treatment of Metastatic Carcinoma in Regional Lymph Nodes —**  
**Indications for Dissection of Regional Lymph Nodes** The regional lymph nodes are never molested unless there is clinical evidence of their involvement by metastatic cancer. Aspiration biopsy of a lymph node may reveal carcinoma and thus establish the indication for treatment, a negative report following aspiration biopsy of a lymph node does not rule out the presence of metastases. The enlarged lymph nodes may subside if the infection in the primary cancer is controlled by hot antiseptic dressings but never if metastases are present. It is a safe rule to suspect all enlarged regional nodes of containing metastatic carcinoma until proved otherwise.

**Surgical Treatment** The dissection of cervical or inguinal nodes should be complete. This dissection never precedes the treatment of the primary cancer and is seldom done at the same time. The usual procedure is to treat the primary cancer first by surgical excision or radiation therapy, when the wound has healed or the irradiated cancer exhibits satisfactory regression, the dissection of the lymph node-bearing region is performed. The interval between these procedures varies from one to three weeks.

**Radiation Therapy** Metastatic squamous cell or spindle cell carcinoma cannot be cured by irradiation alone. If the diagnosis has been proved by aspiration of the enlarged nodes or if the presence of metastases in the nodes is strongly suspected, radical dissection followed by postoperative irradiation is the method of choice. Such radiation therapy is given prophylactically, not with the hope of sterilizing residual cancer but to induce fibrosis in these tissues, prevent the reformation of new lymphatic channels and possibly exercise a restraint on the growth of any viable cancer left after the dissection.

Individual cervical nodes containing metastatic carcinoma, if inoperable or occurring in patients unsuitable for operation, may be treated by external irradiation with the protracted divided dose technic. The roentgen rays are applied with the following factors: 200 kilovolts,

0.5 mm copper and 1 mm aluminum filtrations, 50 cm target-skin distance, circular ports through cones to encompass the involved nodes only and daily fractional doses of 200 to 300 r until each port has received from 2,000 to 3,600 r units

After the completion of external irradiation, supplementary interstitial radiation therapy may be used by the insertion of gold radon seeds in measured tissue doses. This treatment is more successful for cervical nodes containing metastatic carcinoma, because these nodes have strong capsules which restrain the carcinoma within the node. The axillary and inguinal nodes have delicate capsules often infiltrated by fat, metastatic cancers in these nodes may perforate the capsule early and invade the loose fat of the axilla or groin, thus defeating most attempts at control by irradiation. The involved lymph nodes, especially in the cervical group, are exposed through a limited incision so that one may implant the radon seeds or small radium needles with greater accuracy.

## CUTANEOUS CANCER FROM THE POINT OF VIEW OF THE RADIOLOGIST

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**T**HE indication for type of treatment in cancer of the skin will depend on the following factors age, life expectancy, location, occupation, invasion of bone and cartilage, previous treatment, nature of the tumor bed and previous trauma and its presence in scars

Regardless of the type of neoplasm, in very aged persons and others whose life expectancy is short, cure is often sacrificed for palliative effect Therefore, for many patients for whom surgical excision rather than radiotherapy might be indicated, the latter treatment would be the method used

Carcinomas of the scalp or the extremities are usually treated better by surgical means This is especially true for those of the feet and in the pretibial regions Radiotherapy for young patients should not be used on parts of the body where there will be constant irritation or on exposed parts, such as the face and more especially the ears, which will be exposed to extremes of weather, especially cold and intense sunlight

Cancer resulting from roentgen ray burns and cancer in scars from other burns do not as a rule do well with radiation therapy However, numerous small lesions, less than 1 cm in diameter, can be successfully eradicated by radiotherapy The results with radium therapy have not been uniformly good, especially in the early days before the establishment of the gamma "r" unit of measure It has been found that roentgen rays are more easily applied and that the results are superior This has been borne out in an experience of over 300 cases of cancer involving all parts of the body and of both squamous cell and basal cell types It has been found that everything else being equal it is no more difficult to eradicate a primary tumor if it is a squamous cell than if it is a basal cell cancer

The management of metastatic lymph nodes is mainly a surgical problem However in cases in which this is contraindicated, long

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palliation and a possible cure may be obtained by radiologic means (roentgen rays and intrinsic radon implantation)

For lesions 0.5 cm in diameter or smaller, a single treatment of 3,000 or 3,600 r is used. For larger lesions up to 3 cm in diameter the dose is five times 900 r (80 to 100 kilovolts) given within ten days. When contact therapy is used (45 kilovolts, filter of 1.2 mm of aluminum and focus-skin distance 4.1 cm), six times 1,000 r is the dose. With this technic the rate of cure among patients with primary tumors not previously treated was over 90 per cent.

It has been found in general that invasion of cartilage is not a contraindication to radiotherapy unless the patient is exposed to extremes of temperature and sunlight, which may bring about the breakdown of the scar at the site of the treated lesion. There is no advantage in electrocoagulation or desiccation of the lesion before roentgen ray therapy. A careful setup with the use of lead cut-outs over the lesion allowing a minimum of 0.5 cm of healthy tissue around small lesions and larger areas of healthy tissue around larger lesions has been found to be a practical necessity for a high percentage of cure.

## RADIOTHERAPY OF EPITHELIOMA OF THE SKIN \*

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**T**HE treatment of epithelioma of the skin by roentgen rays and radium is influenced by the accessibility of the growth to irradiation, by its radiosensitivity (as contrasted with the radioresistance of the normal tissues included in the irradiated field) and, finally, by the dosage and the technic of radiotherapy

### ACCESSIBILITY

Ninety-eight per cent of the basal cell and 75 per cent of the squamous cell epitheliomas of the skin are located on the head or neck, while 2 per cent of the basal cell and 25 per cent of the squamous cell cancers are found on the trunk and extremities. Basal cell epitheliomas usually grow slowly, often remain flat and show central excavation, and, except in certain locations, they rarely invade subjacent tissues and do not metastasize to regional nodes. Squamous cell epitheliomas are more likely to proliferate without undergoing necrosis, to form bulky growths or to invade and they metastasize in about 18 per cent of the cases.

Because most epitheliomas of the skin are treated while they are still small and accessible, all types of therapeutic procedures are often successful. Curability decreases with increasing size of the growth on the surface, especially if the epithelioma tends to invade subjacent tissues or to metastasize.

"Invasive" epitheliomas are more likely to have silent extensions and if they are squamous to have regional metastases. A special tendency to invasive growth of basal cell epitheliomas is noted if they are located at the inner canthus of the eyelids or at the edge of the nostril and if they are located on the forehead, a site more common in women. Squamous cell epitheliomas with invasive tendencies are found on the pinna of the ear (mostly in men), in the external auditory canal (chiefly in women), on the dorsum of the hand and at mucocutaneous junctions, e. g., the lower lip, the anus, the vulva and the penis.

\* At the request of the editor, all references have been omitted for the sake of brevity.

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Accessibility and radiocurability depend on the location, the extent on the surface and, more especially, the depth of the primary growth as well as the presence or absence of involvement of regional lymph nodes

#### RADIOSENSITIVITY OF TUMOR

The second factor governing radiocurability is the inherent radiosensitivity, i e., the immediate response of the tumor as contrasted with the radioresistance of the normal tissues included in the irradiated field. The importance of this factor is best appreciated in the treatment of extensive epitheliomas, as small epitheliomas are frequently overirradiated and destroyed, irrespective of their inherent radiosensitivity. Basal cell epitheliomas may regress with a slightly smaller dosage of radiation than that needed for well differentiated squamous cell growths of the same extent. Some poorly differentiated squamous cell epitheliomas, however, regress as readily as do basal cell tumors, e g., bulky epitheliomas developing in sebaceous glands in the preauricular or masseteric regions. More radioresistant and preferably not treated by radiotherapy but by excision are the rare adenocarcinomas and adenocystic epitheliomas arising in sweat glands. In exceptional circumstances, however, radiotherapy may be preferable to operation, or vice versa, in cases in which this treatment ordinarily would not be employed.

#### RADIORESISTANCE OF TUMOR BED

The normal tissues included in the field of irradiation are exposed to the same dose of radiation as the tumor. Whenever possible, therefore, radiosensitive normal tissues should be excluded from the irradiated field. For instance, in roentgen ray therapy of epitheliomas of the eyelids, the globe is protected by inserting lead shields under the lids. Special lead shields are used to shield the testes when epitheliomas of the skin of the scrotum are irradiated. If such shielding is impractical, the radiosensitivity of the irradiated normal tissues limits the dose which may be administered to the tumor and influences the technique of radiotherapy.

Retrogressive radiation changes of all irradiated tissues normally follow intensive radiotherapy. Injury of the capillary layer at the edge of the rete pegs, i e., about 1 mm below the surface, probably accounts for erythema, exudation, depigmentation and telangiectasia which follow irradiation. Edema, folliculitis and late radionecrosis may represent damage of the coarser capillary layer at the limit of the subcutis, or about 2 mm below the surface. Epilation suggests an effect of radiation at the level of the hair follicles 2 to 3 mm below the surface.

Radiation damage of the tumor and of the normal tissues included in the field of irradiation is proportional to the amount of irradiation and is in inverse proportion to the duration of the treatment. The shorter the treatment, the greater is the damage, provided the total amount of irradiation is the same. The difference in the threshold of radiosensitivity of the tumor and the tumor bed is reduced if the treatment is intensive and short, if, in addition, the dosage is slightly excessive, destruction of the epithelioma may be followed by atrophy and telangiectasia of the irradiated skin. The time when radiation damage becomes clinically appreciable depends on the normal life cycle of the irradiated cells and the intensity of the radiation dose. The larger the radiation dose or the shorter the natural life cycle of the irradiated tissue, the sooner will the radiation damage be recognizable. Thus, intensively irradiated short-lived epithelium of the skin and, more especially, of mucous membranes, will die and desquamate within a few days or weeks after the exposure. Similarly, irradiated long-lived connective tissue or bone may not show any radiation damage for months or even years following the treatment. Dilatation of capillaries with consequent erythema may be seen early after a moderate radiation dosage. With more intensive irradiation, greater dilatation and even rupture of capillaries with interstitial hemorrhage may occur soon after irradiation. Telangiectasia, obliterative endarteritis and hyalinization of the connective tissue take time to develop and may not appear for months or even years after radiotherapy has been completed.

Poorly vascularized skin and subcutaneous tissues do not tolerate intensive radiotherapy well. The interference with the blood supply may have been produced by preceding disease, surgical trauma, intensive radiotherapy or other causes. If vigorously irradiated, this sclerotic tissue may undergo necrosis, as its blood supply is further decreased by the intensive irradiation. This partially explains the poor results of treatment with roentgen rays and radium of lupus, carcinoma, epitheliomas arising on the basis of old chemical or heat burns, most of which are well differentiated, and of scar epitheliomas of all kinds, it partly accounts for the failure of repeated radiotherapy for cancer in which preceding radiation has failed. Surgical treatment is preferable to radiotherapy in most of these cases.

Cartilage or bone adjacent to an ulcerating epithelioma receiving cancericidal doses of radiation may be damaged by irradiation, and chondritis, osteitis or even chondronecrosis or osteonecrosis may develop. This is more likely in such sites as the pinna, nose, chin, forehead and scalp, in which there is little protective soft tissue between the perichondrium or periosteum and the irradiated skin. Occasionally epitheliomas invading the pinna or ala nasi have been cured by irradiation, and those which have not invaded the perichondrium or periosteum



are as curable by radiotherapy as epitheliomas in other portions of the body. The likelihood of radiation damage is increased if the tolerance of the cartilage or bone has been previously impaired by the entrance of bacteria, invasion by epithelioma or interference with the blood supply due to previous operation or radiotherapy. Because of this fact, it is usually better to remove surgically epitheliomas invading cartilage or bone and to exercise special caution if radiotherapy is applied.

Infection, except in persons with uncontrolled diabetes, is not usually a serious problem in radiotherapy of epitheliomas of the skin. Ordinarily the infection is on the surface and disappears with the radiation slough of the tumor. Rarely a streptococcal or staphylococcal cellulitis or lymphangitis has to be cleared up before radiotherapy of the epithelioma is started.

#### METASTASES TO LYMPH NODES

The presence of metastases to lymph nodes from squamous cell epithelioma of the skin reduces the likelihood of a five year cure from the accepted figure of 54 per cent (without nodes) to 18 per cent (with nodes). Radical surgical treatment is preferable if the nodes are freely movable, small and only few in number. Radiation is better if the nodes are multiple or fixed. Roentgen-ray therapy, insertion of seeds or radium or radon needles with or without surgical exposure or the use of teluradium has at times been successful, but more often is only of temporary value.

#### TECHNIC

The technic of the treatment of epithelioma of the skin with roentgen rays and radium is greatly influenced by a consideration of the various factors just discussed. For instance, the extent of the epithelioma on the surface and, more especially, its invasiveness have a bearing on the size of the irradiated field, the target-skin distance and the filter, on the daily and total dosage, on the period of treatment and, finally, on the voltage if roentgen ray therapy is used. The radioresistance of the tumor bed, especially its blood supply, influences the daily and total dosage and the period and repetition of the treatment. Finally, such considerations as the general tolerance and life expectancy of the patient must be taken into account in planning the treatment.

Decision as to whether to choose radium, its emanation gas, radon, or roentgen ray therapy depends on what available source of radiation is best suited for the special location and extent of the epithelioma.

*Radium Therapy* Radium may be used externally or interstitially. Radon may be substituted for the parent element provided its natural 16 per cent daily decay is taken into account.

In external radium therapy there are used special felt, rubber or wax applicators, which may be accurately molded to the outlines of the individual epithelioma, or ready plaques, trays and other applicators of fixed

shape and form, not adapted as precisely but nevertheless satisfactory for some epitheliomas which happen to fit the shape of the applicator. Applicators made of Columbia paste (paraffin, yellow wax and wood shavings) or those of dental modeling compound (Kerr) are molded while hot over the part to be treated, they are soft and pliable when heated and become hard and rigid when cooled. If it is practical, it is advantageous to include a bony prominence, e g, the nose or jaw, so as to prevent shifting of the mold during treatment. Tubes containing 5 to 10 mg of radium element or corresponding quantities of radon, filtered through 1 mm of platinum or its equivalent, are distributed on the outside of the mold in accordance with accepted physical rules of the distribution of radiation. The mold is left on for the desired period and then removed.

In a few institutions, 2 to 10 Gm of radium element or its equivalent in radon have been concentrated in large, usually lead-lined, steel containers, called "packs" or "bombs." They have a diaphragmed opening through which the radiation beam is directed, like that of an x-ray tube. This type of telerradium therapy is useful in the treatment of metastases to lymph nodes and occasionally for deeply invasive epitheliomas.

For interstitial irradiation either needles or seeds are employed. The short active length of the gold or platinum seed (0.5 cm) limits its usefulness chiefly to superficial lesions in which homogeneous distribution of radiation throughout the thickness of the tumor is relatively easy, for deeper epitheliomas needles are preferable, as their radiating length may be varied from 1 to 5 cm, according to the thickness of the tumor. Seeds are usually filled with 1 to 2 millicuries of radon, whereas needles contain per centimeter of radiating length anywhere from 0.5 to 10 mg of radium element or a corresponding quantity of radon. Needles have to be removed after the desired period of irradiation, seeds may be abandoned in the tissues, as the radon becomes practically inactive in a month and the seed either sloughs through the surface or becomes encapsulated like any foreign body.

Seeds or needles of appropriate length are inserted into the tissue 1 cm apart. In small lesions they are inserted chiefly into the periphery of the tumor. In extensive epitheliomas additional needles or seeds are inserted into the center of the neoplasm. Allowance must be made for the poorer nourishment of the center of the neoplasm, as well as for the effect of the cross firing when irradiating with multiple needles or seeds in accordance with standard physical rules for the distribution of radiation.

*The Field*—In order to include possible silent extensions at the periphery of the epithelioma, the irradiated field should extend beyond the clinical limits of the growth. Multiple biopsies beyond these limits

may reveal much wider invasion and thus prevent failure of treatment, especially in extensive and in massive epitheliomas. If roentgen ray therapy is used, the width of the zone of apparently normal skin surrounding the cancer should be 0.75 cm. for epitheliomas which are less than 2 cm. in diameter. It should be widened to 2 or 3 cm. and in exceptionally large epitheliomas even to 5 cm., depending on the increasing extent of the epithelioma on the surface and especially on its tendency to invade subjacent tissues. Invasive epitheliomas may show a tiny surface tumor and a wide subsurface extension, like a submerged iceberg.

If radium is used, one should follow the same general principles.

*Target-Skin Distance* In contact roentgen ray therapy of very superficial epitheliomas, the usual target-skin distance is 1.8 to 4.1 cm. For deeper epitheliomas a distance of 15 cm. for fields of diameters of 5 cm. and less and of 30 cm. for larger fields is recommended if 100 to 135 kilovolts is used. For extensive invasive lesions, a target-skin distance of 50 cm. and 130 to 200 kilovolts are usually preferred. The target-skin distance for fungating lesions should be measured from the level of the skin and not from the top of the fungating neoplasm. The fungating part of the neoplasm is thus overirradiated without similar damage to the skin. A hollow radiation cone into which the mass fits facilitates this type of roentgen ray therapy.

In external radium therapy of small noninvasive epitheliomas, the usual target-skin distance is 0.7 to 1 cm. This may be increased up to 3 cm. for the more infiltrating types of growth. In teleradium therapy, target-skin distances of 6 to 14 cm. are employed.

*Filter* Roentgen ray therapy of superficial lesions with 45 to 100 kilovolts is given without a filter or with one of 1 mm. of aluminum, for more invasive epitheliomas, 3 mm. of aluminum and 130 kilovolts, and for those penetrating still deeper, 0.5 mm. of copper and 200 kilovolts are commonly used.

The standard filters for radium have usually been of 1 mm. of platinum or its equivalent for radium tubes, 0.5 mm. of platinum for radium needles and 0.3 mm. of gold for gold seeds.

*Voltage* Most epitheliomas of the skin do not penetrate deeper than the first centimeter, and only few extend beyond 3 cm. below the surface. If 45 kilovolts, a 2 cm. field and 4.5 cm. target-skin distance are used, the depth dose at 0.5 cm. is 40 per cent and at 1 cm. 23 per cent. With roentgen rays of 50 to 60 kilovolts, that is, 0.9 angstrom, 87 per cent of the radiation is absorbed within the first centimeter of tissue. Most epitheliomas of the skin are probably still treated with voltages of about 100 kilovolts, though for the more invasive types 130 or 200 kilovolts is preferred.

*Repetition of Treatment* If one hopes to cure an epithelioma, a single irradiation treatment is given. This first and only treatment may consist of one exposure or of a series of exposures, but once completed it is never repeated unless the epithelioma has persisted or has recurred. This is done so as to avoid reirradiating previously treated normal tissues forming the tumor bed. The retrogressive radiation changes in normal tissues occurring after intensive radiotherapy have been discussed under the heading of "Radioresistance of the Tumor Bed." If a cure is not expected, weak radiation intensities are repeated from time to time in order to restrain growth and relieve symptoms. Repetition of such sublethal noncancericidal doses every few weeks or months, however, does not destroy cancer completely. The cancer cells which are not killed reproduce between treatments and present a front of fresh, undamaged daughter cells when the growth is again irradiated. The blood vessels and connective tissue of the tumor bed, on the other hand, are not replaced by new ones but cumulate the damage of each successive exposure and finally succumb, undergoing radionecrosis. In attempts at curative radiotherapy, all treatment is therefore completed before noticeable retrogressive radiation changes have taken place in the irradiated blood vessels and connective tissue, i. e. within two or two and a half months. These normal structures, then, are able to tolerate the damage of this first and only series of intensive radiotherapy.

*Criterion of Adequate Dosage* A cancericidal dose for each variety of epithelioma has as yet not been accurately determined. For all epitheliomas it is therefore customary to administer a radiation dose which will destroy the epithelium from which the epithelioma originated and yet allow the corium to live, so as to permit reepithelization of the denuded area of skin. Irrespective of the technic of irradiation, correct irradiation should produce a complete wet desquamation of the irradiated epidermis leaving under it a denuded, raw bleeding corium. Healing after denudation occurs by ingrowth of epithelium from the edges just outside the irradiated field and from a few epithelial cells in the depths of the hair follicles, which escaped destruction by the radiotherapy. The speed with which healing takes place depends on the size of the denuded area which has to be covered and the radiation damage to the underlying blood vessels. Healing is prompt in small areas and slower in larger ones and may take from one to several weeks. Epithelization may be slow or even inadequate to cover the defect if the amount of irradiation has been too great, if it was given in too short a time, if the field has been too large or if the nourishment of the normal tissues included in the irradiated field has become impaired. In extreme circumstances pinch or even pedicle grafts are needed to cover the nonhealing denuded area. Epitheliomas have been cured with lower dosage and without wet desquamation, yet I should not like to recommend this method.

On the other hand, wet desquamation only denotes adequate dosage at the level of the desquamation and gives only indirect information as to the sufficiency of radiation below this level. Though the threshold of the radiation dose which will produce a wet desquamation is narrower and therefore more reliable than that which will cause an erythema, it indicates only the minimal and not the maximal dosage which has produced this reaction.

*Massive Versus Fractional Radiotherapy* Decision as to whether to administer the entire dose in one exposure or to fractionate it into several treatments depends on the size and vascularization of the irradiated area. The shorter the period of treatment, the greater the effect on the tumor, but also the more damaged are the blood vessels and the connective and other normal tissues included in the irradiated field. If one administers the entire dose in one massive exposure, there is less difference in the injury to the tumor and tumor bed than if this dose is fractionated. In this form of radiotherapy, destruction of the epithelioma may be accompanied by destruction of the normal tissue included in the field of irradiation. Massive therapy is therefore confined to small fields located in nonvital areas and may be used for the average superficial basal cell epithelioma 1 to 2 cm or less in diameter. Fractional radium or roentgen ray therapy may be as effective in the treatment of cancer as massive therapy is, yet it spares the normal tissue more. It is preferable to the massive method of treatment when the tolerance of the tumor bed is low, the field to be irradiated is large and repetition of exposures is not inconvenient to the patient. Fractional therapy would be chosen for treatment of epitheliomas near cartilage, as massive therapy would be more likely to cause chondronecrosis.

*Total and Daily Dosage* Dosages vary in different clinics. The total dose is increased if the size of the field is made smaller. With contact roentgen ray therapy in so-called "caustic irradiation," single doses of from 6,000 to 12,000 r have been administered and good healing has resulted. Three thousand roentgens with 100 kilovolts, 15 cm target-skin distance and no filter (half-value layer-1 mm of aluminum) for basal cell epitheliomas 1 cm in diameter has yielded satisfactory results. A total dose of 4,000 to 6,000 r, depending on the size of the field, fractionated into daily dosages of 250 or 500 r every other day leaves a better scar and may be more effective. With 130 and 200 kilovolts, smaller daily and total doses are needed, in view of the greater volume of irradiated tissue and the increased scattered irradiation.

With external radium mold therapy at 0.7 cm target-skin distance, 1,000 milligram hours and a filter of 1 mm of platinum to a 2 by 2 cm field used to be a standard dosage. Nowadays 4,500 to 7,000 r of gamma radiation is usually given to fields of various sizes.

Teleradium dosage varies with the target-skin distance and the size of the field. In interstitial therapy, 1 millicurie destroyed or 133 milligram hours per cubic centimeter of tissue was formerly the standard. Nowadays one attempts to obtain in from five to ten days a tumor dosage of 4,000 to 6,000 r of gamma rays for basal cell epitheliomas and from 6,000 to 7,000 r for squamous cell epitheliomas.

*Operation or Radiotherapy.* Decision as to whether a particular epithelioma should be treated by radiotherapy, electrocoagulation, application of zinc chloride or excision depends on the experience and skill of the person making the decision, on the availability of the proper equipment and on the extent and location of the epithelioma. Radiotherapy might be preferable for parts of the body where resection and plastic repair would be deforming, e. g. on the nose. Surgical treatment would be better than radiotherapy in most cases with invasion of fibrous tissue, bone or cartilage, e. g., in deep or extensive epitheliomas of the scalp, auricle, etc. It would be preferable where the tumor bed is poorly nourished, e. g. in epitheliomas on the basis of an old lupus or a burn or after failure of radiotherapy, especially if telangiectasia and atrophy are present. Electrocoagulation might be chosen as a palliative measure in the treatment of an inoperable lesion recurring after radiotherapy. As far as curability of the average epithelioma is concerned, it is immaterial whether one uses radiotherapy or surgical intervention provided adequate treatment is applied to all cancer cells. Success depends on the appreciation of the extent of the growth and its adequate treatment during the first and only treatment.

#### SUMMARY

The use of roentgen ray and radium or radon for the treatment of epithelioma of the skin is influenced by the accessibility of the growth to irradiation, by its radiosensitivity as contrasted with the radio-resistance of the tumor bed and, finally, by the dosage and technic of radiotherapy as discussed in the preceding pages.

# GROSS PATHOLOGY OF CUTANEOUS CANCER

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IN THIS brief survey, the biologic characteristics of the principal malignant epithelial neoplasms of the skin will be presented from the point of view of gross morphology and its importance in diagnosis, prognosis and treatment. Melanomas will be excluded, and the group to be considered will consist of basal cell and squamous cell epitheliomas, including Bowen's disease, and carcinomas of sweat and sebaceous glands. An idea of the relative frequency of these tumors may be gained when it is stated that during a ten year period there were recorded in the laboratory 1,224 malignant tumors of the skin. 605 of these were basal cell cancers, 309 were squamous cell tumors, including Bowen's disease, 21 were sweat gland carcinomas, and 2 were sebaceous gland cancers. The remainder consisted of 150 malignant melanomas, 55 sarcomas and 82 secondary neoplasms.

In order to obtain a broad general view of cancer, one should visualize it as starting from a focal point or occasionally from several focal points and growing centrifugally in all directions. For some reason not understood, the growth and spread does not take place at an equal rate in all directions in every tumor but tends to expend its chief growth energy in one of three different directions. For the skin these are first, outward from the body surface and at right angles to it, producing a projection, second, in the exact opposite direction that is penetrating inward into underlying tissues producing early ulceration and, third, parallel with the body surface, either within the epidermis alone or involving both epidermis and papillary layers. There are, of course, exceptions in which a tumor may display two or even all three of these growth characteristics in equal degree, but the majority can be so divided.

These features account for the gross appearance of the tumors and have some bearing on their treatment and prognosis. Of the squamous cell cancers, the deeply penetrating ulcerating tumors are most often seen in irradiated and other scarred areas while the spreading superficial

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This paper is the seventh in a "Symposium on Diagnosis and Treatment of Cutaneous Cancer," held at the New York Academy of Medicine, Section of Dermatology and Syphilis, on April 4, 1944

tumors include Bowen's disease and other intraepidermal epitheliomas. In the case of basal cell cancer, the deeply infiltrating tumors are the rodent ulcers and the superficial spreading ones are the multicentric basal cell epitheliomas and self-cicatrizing "field fire" tumors. Of the much rarer sweat gland and sebaceous gland carcinomas, examples of the spreading form have not been described. Many of the tumors are projecting, a few infiltrating and some a combination of the two.

In general, one can say that as a group the infiltrating tumors are the most malignant and hardest to eradicate. The projecting tumors are much less malignant and much easier to cure because of the absence of deep penetration. The superficially spreading tumors are also less malignant and present no difficulties so far as deep penetration is concerned. The question of metastasis seldom arises, except in the case of squamous cell epithelioma. Here the rule holds, for it is the deeply penetrating ulcerated squamous cell tumors which most frequently metastasize. Metastases from basal cell epitheliomas and sweat gland and sebaceous gland carcinomas are so rare that no generalization about them is permissible. There are records of two examples of metastasis in each of these three types of tumor in the laboratory of surgical pathology of Columbia University. Most of them occurred in tumors which both projected and infiltrated.

It must be emphasized that this statement is not intended to express an inflexible rule but is simply a possibly useful generalization about the growth tendencies of these malignant tumors.



# HISTOPATHOLOGY OF CUTANEOUS CANCER

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**I**N a brief review of a large subject, only the important features can be enumerated with little or no explanation of many others being made. Therefore, I believe, I need not consider the adnexal neoplasms, as syringoma, trichoepithelioma, multiple benign cystic epithelioma and the others. These are either nevi or nevoid lesions and are not malignant.

Epitheliomas of the skin are epithelial neoplasms which are malignant. There are three large groups, depending on the cells involved: basal cell, prickle cell and undifferentiated cell. These may be subdivided into intraepidermic and extraepidermic, and these, in turn, may be either "en masse" or "disseminated."

Basal cell epithelioma may occur anywhere on the skin and even on the mucous membrane. The growth is composed entirely of basal cells which have hyperchromatic nuclei and only a small amount of cytoplasm, and the cell outlines are not present. While normal basal cells contain prickles, those of the neoplasm do not. There may be some mitotic figures, but they are not abundant. The tumor may come from one point or many points (multicentric). This is of little import except in the case of superficial basal cell epitheliomatosis. It may take on any configuration, even simulating that of glandular tissue. Pigment and cystic formation may or may not be present.

Spinobasal cell epithelioma is synonymous with intermediary or transitional cell epithelioma. This type, in the main, is a basal cell epithelioma, within which there may be some whorls and pearls, and prickles are seen in some areas.

Epitheliomas developing in the sweat apparatus are of the basal cell variety. These may develop from the duct or from the glandular portion.

While it is generally agreed that the spinobasal cell epithelioma can and at times does metastasize, it is doubted by many that this can take place in a pure basal cell variety. However, I believe that even this type does metastasize, as I have specimens to show such occurrence.

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The term "prickle cell epithelioma" is more scientific than "squamous cell epithelioma." As squamous cells cannot proliferate, naturally they cannot give rise to a neoplasm. However, the term has been used so long that it is still retained. The diagnosis of this variety depends not only on the hyperplasia of prickle cells but on the evidence of malignancy in them, such as whorls, pearls, keratinization, mitotic figures, anaplasia and dyskeratosis. Pearls, keratinization and accelerated dyskeratosis are present in the less malignant epithelioma, while whorls, mitotic figures and retarded dyskeratosis are to be seen in the more malignant epithelioma. In grading prickle cell epitheliomas one must consider not only Broder's classification but the aforementioned evidences of malignancy. For classification of a carcinoma grade 4, regional lymph nodes should be present.

In considering the malignancy of basal cell and prickle cell epitheliomas, one must pay special attention to the state of the palisade layer and also to the inflammatory protective zone. When the palisade layer is intact, the neoplasm is intraepidermic and therefore "en masse", with a disruption of this layer the neoplasm is extraepidermic and either "en masse" or "disseminated." It is then clear that with an intact basal cell margin, regardless of the type, the tumor is relatively benign and there is no opportunity for metastasis.

The inflammatory zone beneath the growth is considered by some as one of the predisposing factors for the development of the tumor. Others, however, feel that it is a protective mechanism. I agree with the latter group and feel that a productive inflammatory zone is present in the less malignant neoplasms while the exudative protective inflammatory zone indicates a more malignant process. The inflammatory protective zone is an aid not only in diagnosis but in prognosis.

The last, and most malignant, group is that of the anaplastic, embryonic or undifferentiated cell epitheliomas. In general, the cells are large, with large deeply stained nuclei, a considerable amount of cytoplasm, which becomes somewhat granular, and distinct cellular outlines. The cells are usually round and have many mitotic figures. When the cells divide by amitosis, rather than mitosis, the malignancy is increased.

Of this group the least malignant is Bowen's tumor, a neoplasm which is rare. It develops from preexisting Bowen's disease. The cells are large but vary in size. They have many multinucleated cells (Bowen's cells), and frequently there is a clear cytoplasm. The prickles are lost.

The next group is that of the anaplastic epitheliomas which may arise directly from the epidermis or from the periphery of a previous basal cell or prickle cell epithelioma. When the tumor arises directly from the epidermis, it is frequently from a senile keratosis. Lesions

on the mucocutaneous junction often show evidences of malignancy without neoplastic development. These do go on to anaplastic epithelioma. Of course, one must be careful to rule out pseudoepitheliomatous changes.

Paget's tumor develops from either the epidermis or the ducts or both. Although many authors have reported extramammary primary Paget's disease, I do not believe that this occurs. There is considerable doubt whether the reported cases were not cases of Bowen's disease rather than of Paget's disease.

There are some terms that need a few words of explanation. I do not use the term "epidermoid carcinoma." A carcinoma may originate from the epidermis or follicle, some come from both. In general, those from the follicle wall are not so malignant as those from the epidermis. Instead of stating that a carcinoma (epithelioma) develops in situ, I use the terms "intraepidermic" or "extraepidermic." The term "spindle cell epithelioma" is a misnomer. In many instances in which the tumor is large or is growing into fibrotic tissue the cells will become compressed and flattened and appear spindle shaped.

The classification of epithelioma of the skin into basal cell, prickle cell and anaplastic cell is given in order of their degree of malignancy. While there may be considerable overlapping in specific instances, in general the classification is correct. The degree of malignancy varies from relative benignancy to highest malignancy. The epitheliomas of slightest malignancy are of such a nature as to make some authorities believe that they belong among the nevi rather than among the carcinomas.

Finally, in many cases the pathologic picture is necessary not only to make a diagnosis of epithelioma but to show the variety and activity of the lesion and, therefore, is most essential in the prognosis and successful treatment of the disease.

## DISCUSSION

ON PAPERS OF DRS. TRAUB, ANDREWS, WEBSTER, PACK, HARRIS,  
LENZ, STOUT AND SACHS

DR. ANTHONY C. CIPOLLARO, New York. It has been a great privilege to listen to so many renowned experts in the field of cancer. Although it is difficult to discuss all these papers, I shall reiterate some of the more important points pertaining to the general subject of cutaneous cancer.

Drs. Stout and Sachs have described the essential features of the main varieties of cancer and in the main are in agreement on all important details. I think that in a discussion of cancer of any organ or of any type it is always important to emphasize the danger of metastasis. It is true that basal cell epitheliomas do not metastasize except in extremely rare instances, as Dr. Stout said, but squamous cell epitheliomas do metastasize, especially when they are either neglected or poorly treated. Bowen's disease has been considered to be a precancerous dermatosis, but, as Dr. Stout pointed out, it is a true intraepidermic epithelioma and occasionally it may take on characteristics of a squamous cell epithelioma.

Dr Traub classified the clinical types of basal cell epitheliomas. This classification is important not only in visualizing the various clinical types but in evaluating their course. I am sorry that I have to disagree with a few minor details. Extensive lesions of basal cell epitheliomas on the eyelid, in my opinion, are better handled by a surgeon. No one can doubt the excellent results obtained by Dr Traub in the treatment of this and other types of extensive basal cell epitheliomas, but I doubt that there are many dermatologists who are as skilled as he is in handling these cancers with electrosurgical eradication. Small lesions on the ear, even of the squamous cell variety, rarely if ever metastasize and are well handled by electrosurgical destruction. I have found that the multiple superficial type of basal cell epitheliomas is resistant to radiation, and my preferred method of treatment is with electrosurgical excision and curettage under procaine hydrochloride anesthesia.

Drs Pack and Webster adequately emphasized the importance of selection of cases. Not all cutaneous cancers are amenable to the same type of treatment, even to the same type of surgical procedure. The many factors, such as age of patient, duration, location and size of lesion, type and grade of malignancy, previous treatment and type of soil from which the epithelioma arises, are important considerations in the selection of the proper method of treatment. Dr Webster is right when he states that the healing period is long after electrosurgical procedures. I agree with him, but against these disadvantages there are certain advantages of electrosurgical procedures, some of which have already been mentioned by Dr Traub. Some of the advantages are the elimination of hospitalization and general anesthesia and the minimizing of shock, nervous tension and expense. Most electrosurgical procedures can be carried out in an office with procaine anesthesia, just as any simple minor operation is.

Dr Harris showed that many cutaneous cancers which can be adequately treated by surgical procedures also can be treated with irradiation. He also discussed in a limited way the mechanics and the physics of roentgen ray therapy. He is particularly partial to contact therapy for the treatment of superficial cancer. Since Dr Harris brought up the question why dermatologists do not use contact therapy oftener, it may be well to mention a few reasons. Contact therapy is of limited usefulness in dermatology. It is useful only for small lesions, such as cutaneous cancers, warts, keratoses and other small similar lesions, because the field of irradiation is small. Most of the dermatoses that a dermatologist is called on to treat are generalized, and contact therapy apparatus would be inadequate for this purpose. Another reason why it is unnecessary for a dermatologist to have an extra expensive machine in the office is that practically everything that can be done with a contact therapy apparatus can also be done with a modern shock-proof machine. The only possible difference is that instead of delivering a cancer-killing dose in twenty to thirty seconds it may take a minute or two. In other words, the increased intensity obtainable with the contact apparatus can also be obtained with a modern shock-proof apparatus by decreasing the distance between the surface of the lesion and the anode.

I do not believe that dermatologists should minimize the danger of either an acute or a chronic radiodermatitis. One must bear in mind, as statistics show, that in about 25 per cent of the patients with radiodermatitis cancer develops. Many dermatologists over a period of years have experienced, and so have I, that following a single erythema dose of roentgen rays atrophy and telangiectasia developed years later. One should not forget the disastrous results from treating hypertrichosis with roentgen rays. One is justified in obtaining a first or second degree radiodermatitis during treatment of cutaneous cancer, but one is never

justified in obtaining roentgen erythema during treatment of inflammatory dermatoses. It is also my conviction that a simple basal cell epithelioma should not be treated with such intense radiation that radiation ulceration is produced, because a basal cell epithelioma is benign and nonmetastasizing whereas the epithelioma which follows a severe radiodermatitis or a radiodermatitic ulcer is of the squamous cell type and may be metastatic. I do not believe that dermatologists are justified in risking the development of a more serious type of cutaneous cancer in order to cure one of a benign type.

I was glad that Dr. Lenz showed what can happen when a cancer is poorly or inadequately treated. The surgeons as well as the radiologists have stressed the point that cancer must be destroyed completely when it is first seen. Temporizing with a little bit of desiccation or a little bit of roentgen rays or with solid carbon dioxide, with an acid or with the electrolysis needle not only is inadequate treatment but actually subjects the patient to greater danger than if the lesion had been left alone. When a combination method of treating a cutaneous cancer is used, each method must be of sufficient intensity if used alone to destroy a cancer. This brings up the question as to what advantage there is to a combination method. In most instances either surgical treatment which includes electrosurgical procedures or radiation alone is sufficient for practically all lesions. When the two methods are judiciously and expertly combined, the results from the treatment of all types of cutaneous cancers are almost perfect. In rare instances in which the tumors are deeply infiltrating or are inaccessible, a combination of radiation and surgical excision is of inestimable value. Those treating cancer realize that critical judgment based on experience is of the utmost importance in carrying out any treatment aimed at destroying cutaneous malignant neoplasms.

Two of the speakers mentioned the development of basal cell epitheliomas in radiodermatitis and in chemical burns. This must be considered most unusual, because the type of epithelioma which usually develops in radiodermatitis or in chemical burns is of the squamous cell variety. Of course, in radiodermatitis even sarcoma may develop, but this is also extremely rare.

The speakers did not advocate extensive, widespread and heroic surgical treatment for basal cell epitheliomas, nor were excessive doses of roentgen rays recommended for the treatment of these relatively benign cutaneous neoplasms. From their discussion I gathered that the average dose administered for an ordinary epithelioma without metastasis is in the neighborhood of 4,000 r. I am glad that doses of 20,000 or even 10,000 were not recommended. Such tremendous doses for the treatment of cutaneous cancer are never justified, in my opinion.

One further point to be emphasized is that a patient with a severe or dangerous cutaneous cancer is apt to do better when the method of treatment is selected by a cancer team, made up of a surgeon, a radiologist, a dermatologist and a pathologist. Some institutions already have such a setup. It is unfortunate that all those institutions treating cancer do not have such cooperative facilities. It is gratifying to note that mortality statistics of cutaneous cancer have shown an improvement while mortality statistics for cancer of other organs continue to rise.

In summarizing I wish to emphasize particularly the following points: 1. I oppose the extreme measures employed by some in treating basal cell epitheliomas, because there is no necessity for them. 2. Each case of cancer of the skin presents a different problem and requires individualized rather than routine treatment. 3. Some cases of cutaneous cancer require the combined judgment of a cancer team for optimal results. 4. Inadequate treatment is to be condemned.

## AN UNUSUAL CASE OF WARTS

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**T**HE clinical report of this case seems justifiable for various reasons. Because of the lack of treatment, the warty lesions became extensive, numerous and abnormal in size.

On the dorsal surface of each foot there was a veritable warty carapace which covered the whole of the underlying skin surface. Both



Fig 1—Plantar warts in form of mosaic

the finger nails and the toe nails were affected by the disease, the latter more than the former. The inner and outer canthi, which were affected, are not frequent sites for warts. On the palmar and plantar surfaces, besides the large number of warts there was hyperkeratosis. The hyperkeratosis of the palms was due to the patient's occupation—he was a

farm hand while the plantar hyperkeratosis was due to a variety of traumatism caused by the habit of going about barefoot

Neither direct nor cultural mycologic examination showed the presence of fungi. Histopathologic examination showed extensive common



Fig 2—Common warts covering entire dorsa of the feet. Toe nails extensively involved.

palmar and plantar warty growths which were associated with hyperkeratosis.

#### REPORT OF CASE

A. D., a 30 year old unmarried Brazilian farm hand living at Curvelo, in the district of Santa Rita do Cedro, was admitted to Prof. Antonio Aleixo's ward on May 7, 1941.

*Family History*—The parents and five brothers of the patient are alive and healthy. Two brothers had warts which disappeared spontaneously. Collateral relatives are in good health.

*Personal History*—The patient had measles, whooping cough and chickenpox in infancy, but there was nothing else of interest in the history.

*History of the Present Disease*—The patient stated that about fifteen years previously numerous lesions appeared on his forearms, hands, legs and feet, these lesions have persisted.



Fig 3—Common warts on the dorsa of the hands

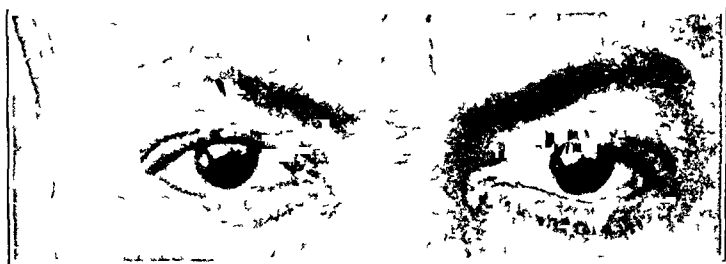


Fig 4—Common warts at the internal angle of the palpebral fissures

*Physical Examination*—General examination revealed nothing abnormal. The mucous membranes were healthy.

*Dermatologic Examination*—The lesions were situated on the forearms, hands, legs, feet and inner and outer canthi of the eyes. All the primary lesions except those on the palmar and plantar surfaces were found to be proliferating monomorphous rounded papules with a grayish surface covered with small erect projecting corneal salients. The papules were firm to the touch and were movable over the underlying plane. They caused no neighboring inflammation and were quite painless. The palmar and plantar lesions were different, because some of them were smooth localized hyperkeratoses while others were hyperkeratoses with



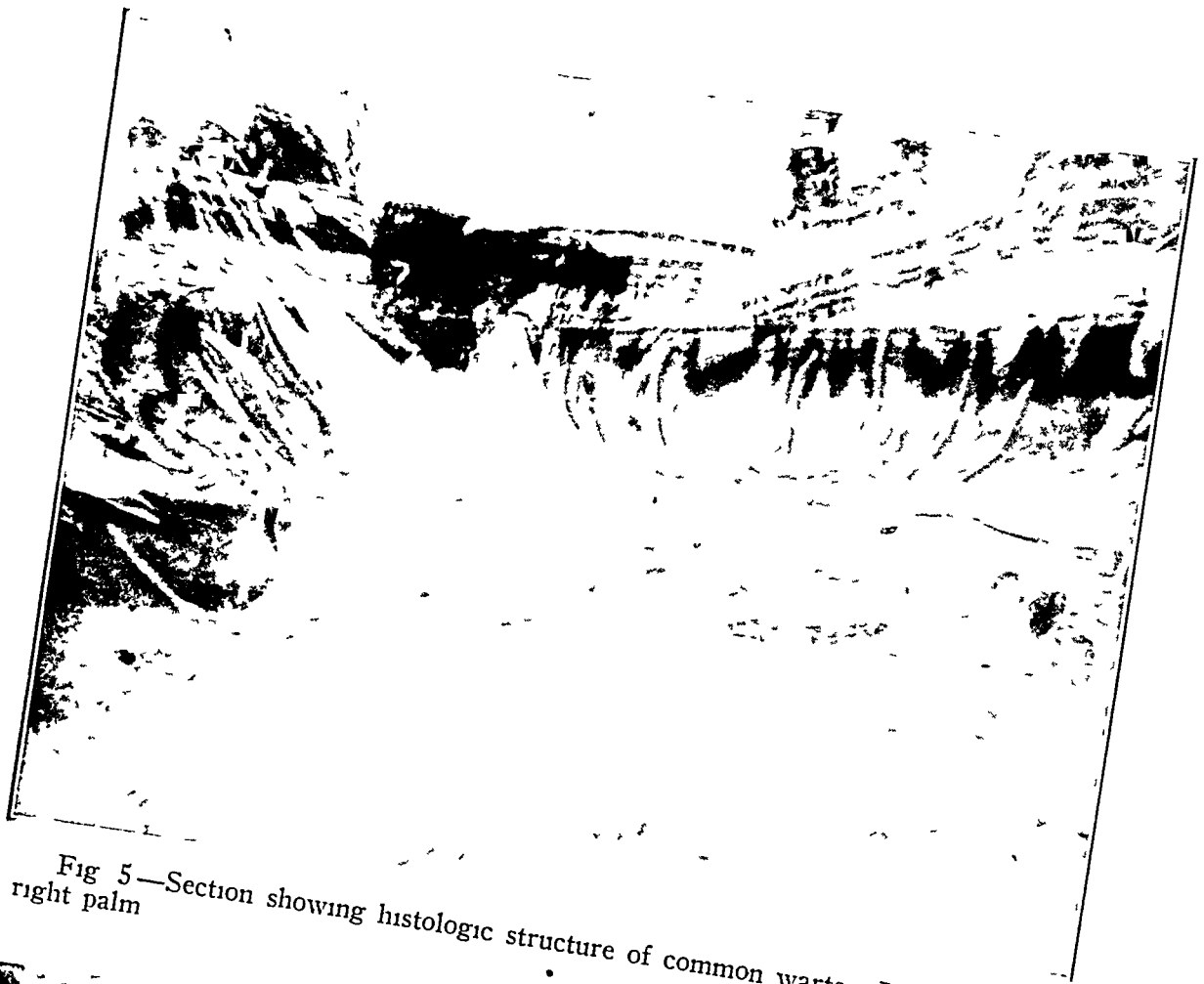


Fig 5—Section showing histologic structure of common warts Lesion on the right palm

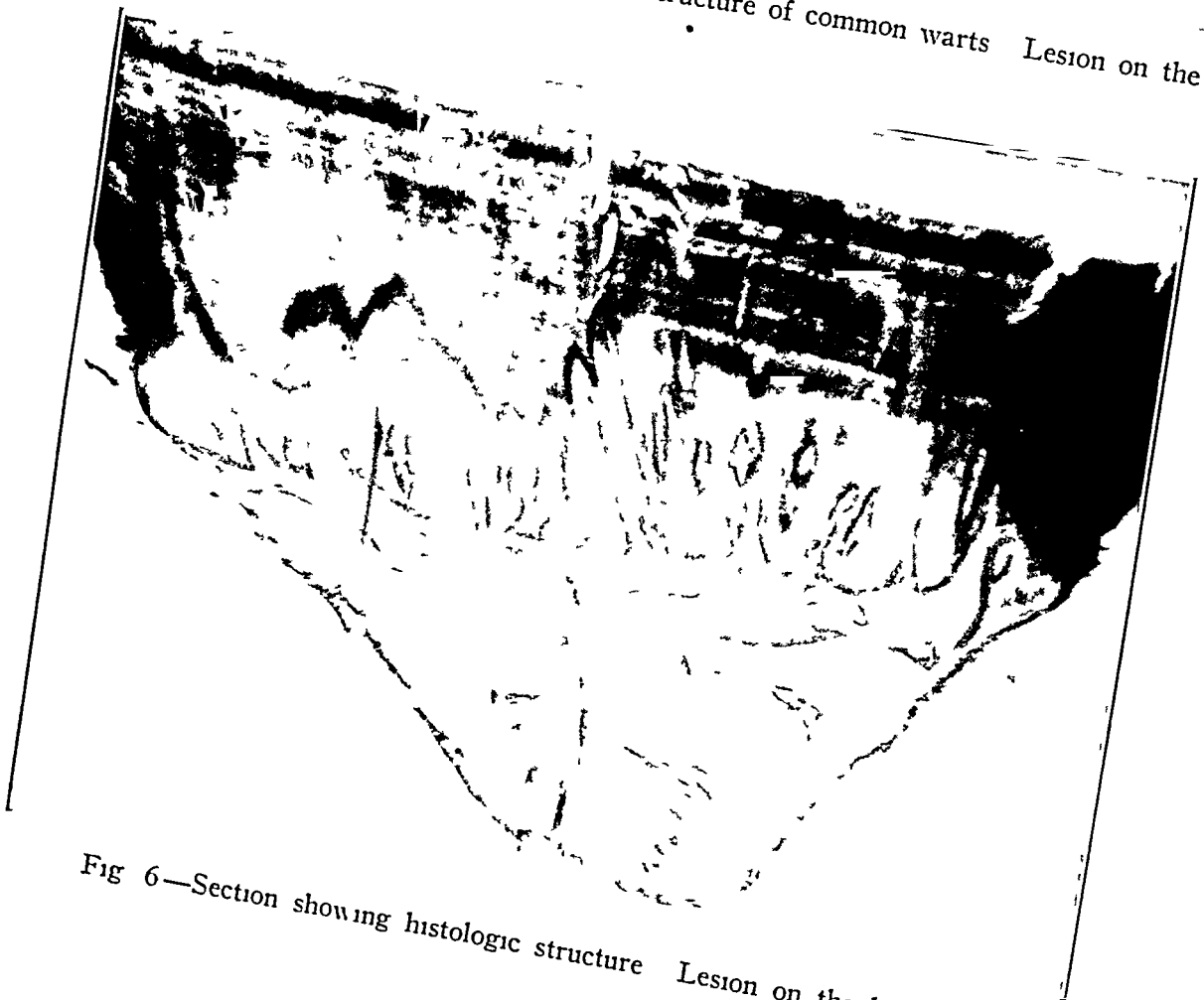


Fig 6—Section showing histologic structure Lesion on the left sole

grooves and hollows. The palmar and plantar lesions were painless, for the patient did all kinds of manual labor and walked barefoot. On each sole there was diffuse hyperkeratosis which at some points showed intersecting furrows and well marked hollows (fig 1). But when the lesions as a whole were analyzed it was seen that they were confluent, completely covering the underlying skin with a veritable warty carapace. Some toe nails were dystrophic, loose from their nail beds and wholly or almost entirely covered with warts (fig 2). Nearly all the nail beds were affected. Grayish slightly raised lesions were seen on the legs,



Fig 7—Section showing histologic structure. Lesion on the dorsum of the left foot.

and there were two gigantic warts on the left knee. There were numerous warts on the backs of the hands, some of them isolated and others confluent, as on the right forefinger, which was completely covered. There were periungual and subungual lesions (fig 3). On both palms the warts were numerous and disseminated, some being smooth and others rough or furrowed. There were two warts at the inner canthus of each eye (fig 4).

*Laboratory Examination*—The Wassermann and Kahn reactions were negative. Direct and cultural examination did not reveal fungi. The histopathologic exami-

nation was carried out by Dr Junqueira, whose report was as follows "In all the specimens the lesions observed were the same—hyperkeratosis, hypergranulosis, hyperacanthosis and papillomatosis. There was slight perivascular infiltration of lymphocytes. In two of the sections, 1 and 3, the rete plugs were longer and flattened (figs 5, 6 and 7).

The anatomopathologic diagnosis was common warts of the palmar and plantar variety.

Rua Ceará, 1691

# EPIDERMOLYSIS BULLOSA SIMPLEX OF THE HANDS AND THE FEET

A Genetic Study of the Hereditary Type

STURE A M JOHNSON, M D \*

Assistant Professor of Dermatology and Syphilology, University of Michigan Medical School  
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ANN ARBOR, MICH

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In 1895 Elliot<sup>1</sup> reported the first of such cases, that of a 30 year old white man who had suffered from the disease since he was 5 years of age. The bullae manifested themselves especially in warm weather. The bullous elevations arose without precedent redness after walking or rowing or after using a hammer or screwdriver. There was an associated hyperhidrosis of the hands and the feet and often bromhidrosis of the latter. There were no subjective symptoms except pain after the bullae had ruptured and left raw surfaces. Examination revealed bullae of all sizes on the hands and the feet, some of which had arisen on the latter during his walk to the consultation. Treatment of many types had been tried but was of no avail. The patient's father had bullae only on the feet.

Lustgarten<sup>2</sup> a year later stated that he had 2 patients who had blisters involving only the palms and the soles. He expressed the belief that these milder types of epidermolysis bullosa were not so rare.

Records of all persons described in this report are on permanent file in the Heredity Clinic, University of Michigan.

Support of this research was provided in part by the Horace H. Rackham School of Graduate Studies.

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This view was also expressed by Waisman<sup>3</sup> Greenberg<sup>4</sup> found an incidence of 0.2 per cent among dermatologic patients seen in an army station hospital during a two year period. More recently, Mooney<sup>5</sup> has reported an incidence of 0.4 per cent.

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the familial features of the bullous disease of the hands and feet. The mode of transmission of the disease was called a dominant, a dominant possibly through a single pair of genes, and a conditional dominant, since it was not known in the homozygous state. Apparently all described simple epidermolysis bullosa transmitted through a dominant gene, since each person cited with bullae had a parent with bullae and since the ratio of affected to nonaffected offspring of a defective parent approached 1:1 when the parents were a heterozygote and homozygote normal. That this dominant is different from the one causing the dystrophic type of epidermolysis bullosa is evidenced by the fact that in no kindred in cases in which the simple form is present does one find the dystrophic form, which is characterized by epidermal changes such as scarring, milia and acrocyanosis. The manner in which the aforementioned kindreds exhibit bullae in the same location, namely

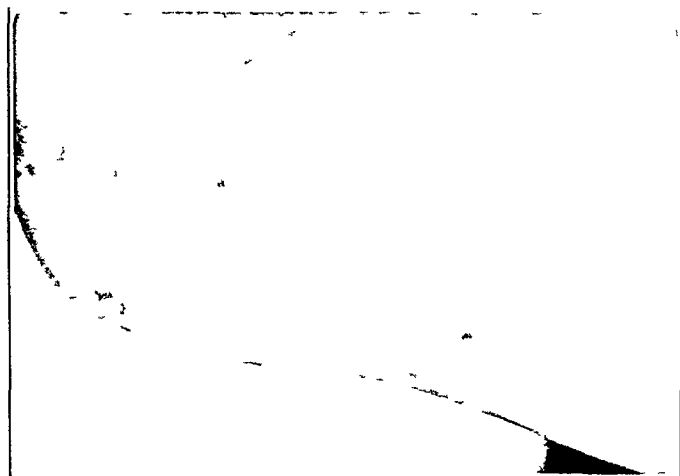


Fig 1—Character of bullous lesions on foot of VI A 14-3, a first cousin of propositus

the hands and the feet, would indicate that one has a genetic entity in the simple type which is as unique in its picture as that, described by Cockayne<sup>11</sup> and others, in which bullae were found only on the feet.

The following report presents another case of epidermolysis bullosa of the simple type involving the hands and the feet, in which a study of the family pedigree uncovered a hitherto unrecognized relationship between the families cited separately by Mansur<sup>13</sup> and by Cartledge and Myers<sup>15</sup>.

#### REPORT OF A CASE

S. D. (VI A 15-3), a white man of Irish-British-Dutch extraction, aged 27, was seen in the outpatient service of the University Hospital on June 11, 1942.

15 Cartledge, J. L., and Myers, V. W. Inherited Foot-Blistering in an American Family, *J. Hered.* 34:24 (Jan.) 1943.



He complained of blisters on the hands and feet. This eruption had been reappearing since infancy, particularly during the hot summer weather. Blisters would occur in the winter after he had played basketball or football for a very few minutes. Many times when there were blisters on the feet there were none on the hands. The chopping of wood or the pumping of gasoline in a service station would cause blisters in a short time. In an area where a blister was going to develop, the patient would sometimes notice a slight burning. There were no sensations after the blisters formed unless the surface was denuded, in which case there was a feeling of soreness and burning. Rupturing a bulla would cause healing in five to seven days, rather than ten to fourteen. Infection or scarring had never occurred. Bullae had never been present elsewhere on the body. The patient felt socially inadequate because of the family stigma under which he suffered.

*Gross Examination*—On the mediodorsal and palmar surfaces of the second and third fingers of each hand as well as on the palm were six to ten tense bullae. There were three bullae on the plantar surface of each foot. The skin surrounding the newer bullae was clear, whereas the skin about the older bullae was erythematous. The roof of each bulla was tense and thin. The newer lesions contained straw-colored fluid, whereas the older ones were filled with a turbid milky material. There were hyperhidrosis and bromhidrosis. There was no scarring, milia, pigmentation or acrocyanosis. The teeth, hair and nails showed no abnormal changes. Nikolsky's sign was not elicited. The results of the physical examination were essentially normal.

*Laboratory Examination*—Examination on several occasions showed the urine to be normal. The hemoglobin content was 85 per cent, and the white blood cell count was 5,400. The Kahn reaction for syphilis was negative. Scrapings of the skin from the interdigital spaces of the feet revealed no fungi, either on microscopic examination of a 15 per cent potassium hydroxide preparation or by growth on Sabouraud's culture medium. Results of similar examinations for the presence of fungi in members of the patient's immediate family (VI A 15-2, -3, -5, -7 and V A 8-1) were negative.

#### FAMILY HISTORY

Many members of the patient's family (fig 2) had suffered from recurrent bullous eruptions limited to the hands and the feet. This disease could be traced back to a forefather who had come from Ireland about 1770 to settle in what is now West Virginia. The tendency toward and the ease of blistering varied in a sibship rather than between sibships. In most members of the family, blistering was slight. This was particularly true as the person became older. Some of the members of the family had been in the armed forces and had been hospitalized for dermatophytosis. Rapid response to rest in bed with immediate recurrence on resumption of marching had resulted in medical discharges from the army without the cause of the bullous condition being recognized. Some members of the family found difficulty in doing manual labor during the summer because of the decided tendency for blisters to develop. Members of the family knew that walking on the hot cement sidewalks for  $\frac{1}{2}$  to 1 mile (800 to 1,600 meters)

would cause blisters of the feet Walking the same distance on the grass or in the dusty street would be less apt to cause trouble Ironing would cause blisters on the hands of many of the housewives Scarring had never taken place in any of the persons who had suffered from bullous eruptions

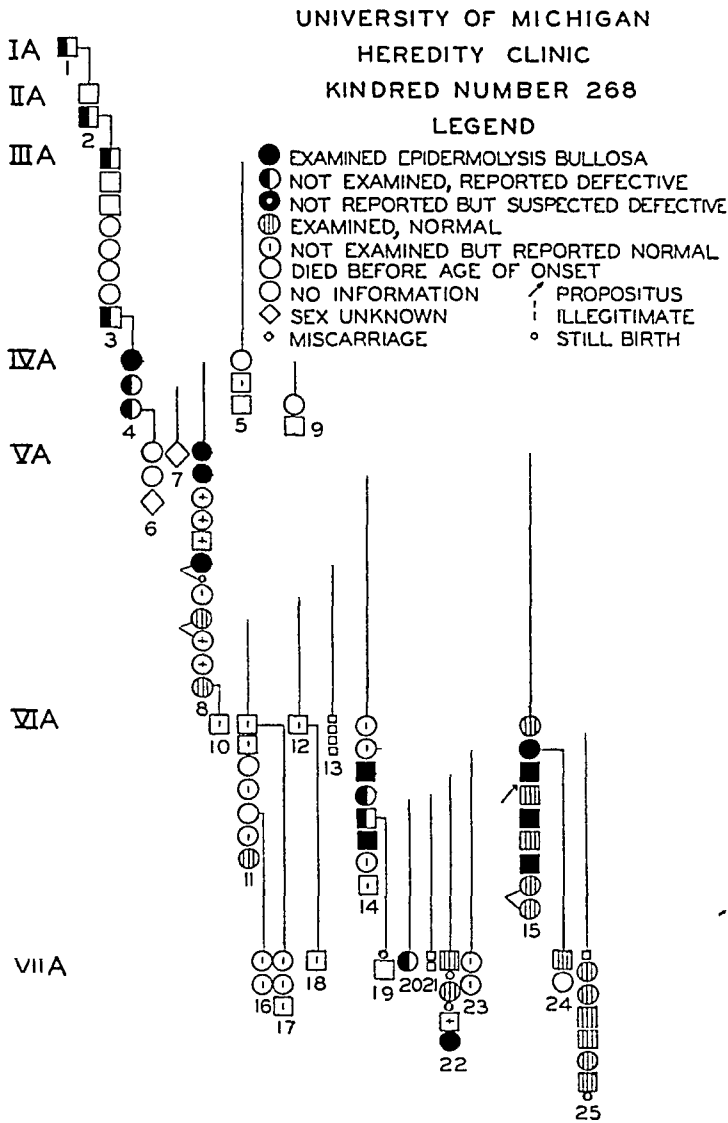


Fig 2—Family tree of family A

These family trees (figs 2 and 3) have been drawn in a style devised by Dr C W Cotterman The sibships are shown in a vertical sequence, with the oldest member within a sibship at the top as number 1, progressing with the order of birth date in series as one passes downward An occasional symbol stands for more than one person, the number of persons then being indicated by an Arabic numeral enclosed within the symbol References will be made to individuals by combining generation numeral and letter A or B for one of the two families, with the sibship number, a dash and then the individual number within the sibship, as IV A 4-3 for the third child in family A, generation IV, sibship 4

Of this family of 105 persons (family A), consisting of seven generations, 10 males and 10 females had suffered from the disease. Whether or not the disease was present in 39 members was unknown, the chances are that none of these 39 who reached adulthood were affected, since we noted that almost everybody was aware of the condition of the persons who had bullae but not of those who did not have bullae. The children of defective parents include 19 affected, 22 normal and

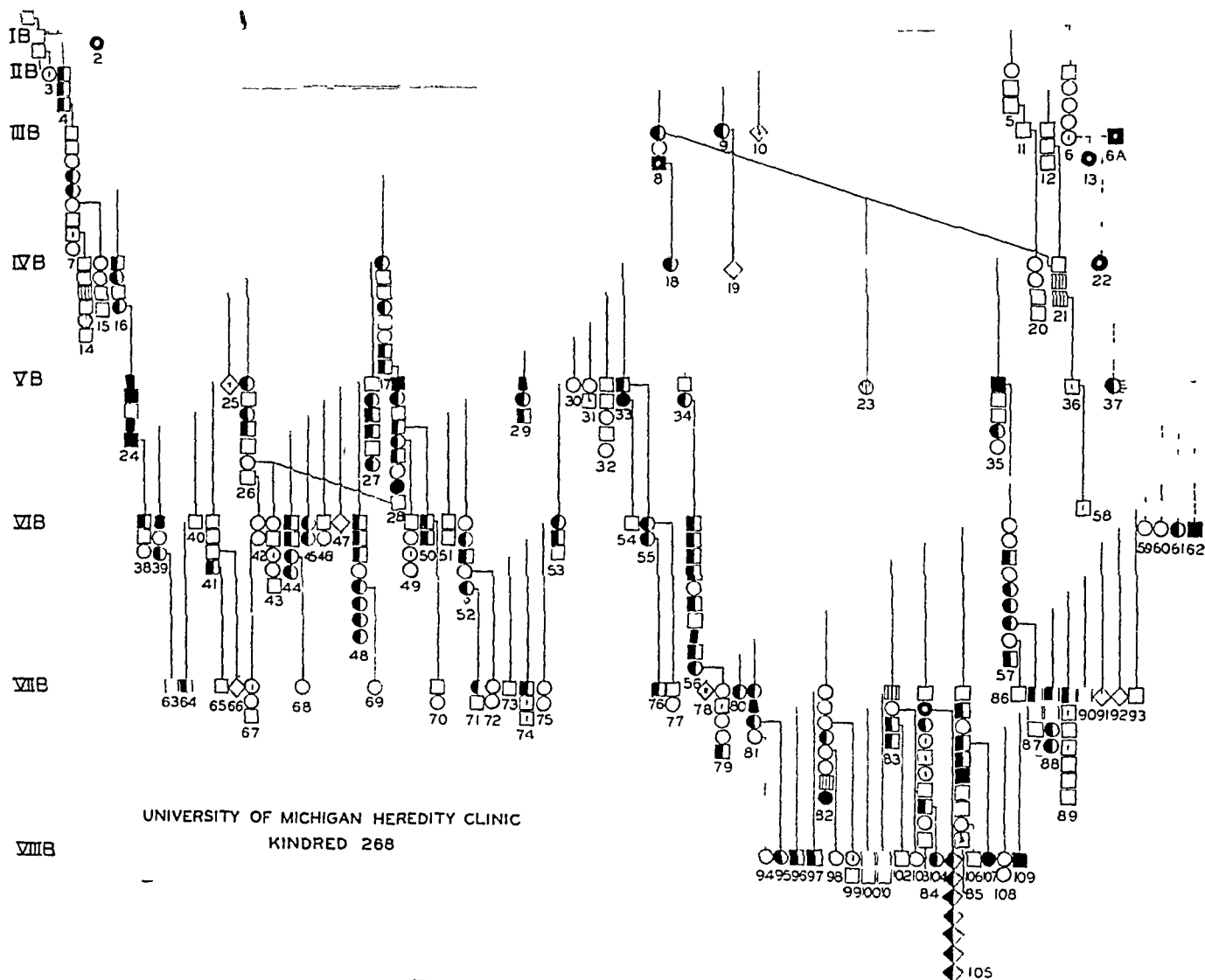


Fig 3—Family tree of family B

39 of questionable status. In every instance in which there was an affected child, a parent was affected. There was no history of consanguinity.

#### COMMENT

Recurrent bullous eruptions of the hands and the feet were referred to as Weber-Cockayne's localized epidermolysis bullosa by Waisman,<sup>3</sup> who stated that Weber described the first case in 1926. It would seem

that credit should be given to Elliot,<sup>1</sup> who in 1895 first reported completely the case of a patient in whom there were bullae only of the hands and feet. Weber's and Cockayne's patients, except in a single instance, had bullae of the feet and not of the hands and the feet.

The variation in severity and the presence of bullae in hot weather have been stressed by Waisman<sup>3</sup> and others. This is apparent in our series. The decided tendency of the bullae to be worse in summer weather and hot weather has caused a recent interest in pathologic porphyrin metabolism and epidermolysis bullosa. Unfortunately, we were unable to study this interesting problem in any of our cases.

A congenital deficiency of elastic tissue has been considered to be the underlying cause of the bullae by some. A biopsy of a member of our group which we studied showed no abnormality of the elastic tissue. This observation has been made by others in the simple form of epidermolysis bullosa. The superficial location of the bullae, between the

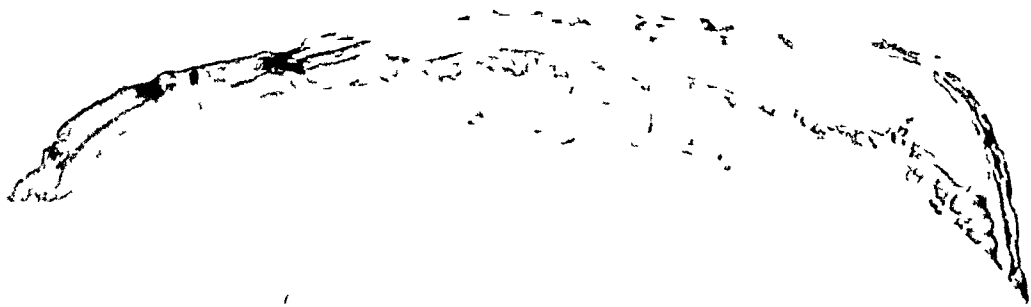


Fig 4—Section from the sole of a 9 month old girl (VII A 22-6) showing hyperkeratosis and parakeratosis. The stratum corneum forms the top of a large bulla which is monolocular and which contains no cells. The stratum granulosum is thickened. There is irregular acanthosis with spongiosis. There is dilatation of the capillaries in the upper part of the cutis. There is perivascular infiltrate of round cells. Weigert's elastic tissue stain of the same tissue reveals no change in the distribution or number of elastic tissue fibers.

stratum corneum and the stratum granulosum, no doubt accounts for the lack of scarring in any of this series.

The tendency of the epidermis to react to local friction, pressure, heat and moisture with bullae—and not with thickening and scarring—is a notable feature. Waisman<sup>3</sup> described this as a passive yielding to the presence of fluid exuded beneath the epidermis to physical irritation. Lustgarten<sup>2</sup> suggested that it was related to factitious urticaria, while Unna, cited by Elliot,<sup>1</sup> said that it was a dermatitis, traumatic in nature, a concept which Elliot also held. On the other hand, Mansur<sup>13</sup> expressed the belief that when the Schneider index was + 11, cutaneous or vascular irritability as an etiologic factor was ruled out.

Whatever the cause of the bullous lesions may be, their varying location on different subjects is indicative of differing genetic entities. It is characteristic of the entire kindred in which a form of epidermolysis bullosa hereditaria occurs that they exhibit bullae in the same location. In other words, bullae may occur only on the palmar and plantar surfaces, in which case they will be found on these surfaces alone throughout the kindred. Or bullae may be found only on the feet, face, elbows or mucosal surfaces.

It was while we were getting data on the persons in family A who resided in Michigan, West Virginia and southwestern Pennsylvania, that we discovered the heretofore unrecognized relationship between the families reported by Cartledge and Myers<sup>15</sup> and by Mansur<sup>13</sup>. At first there was considerable confusion as to whether or not all those in family A and family B were of the same family pedigree. We found ourselves frequently looking up sibships in the family under chart A which belonged to family B. Many in family A or B named as relatives persons whose names appeared on the other chart. The original propositus (VI A 15-3) told us of "some sort of cousins," naming VI B 56-8 and V B 35-5, who blistered. There are certain facts which make relationship between persons in families A and B a probability. The nature of the disease is unusual, and to have two large families bearing the same trait, as shown in figures 2 and 3, living in the same small locality for over two hundred years without there being a common forebear would be most unusual. Furthermore, the surnames of the persons suspected of introducing the defect into the two families I A 1 and I B 2 and the spouse of (III B 6-5) were the same. The frequency of certain unusual given names was striking and suggestive of relationship. The first person reported to show the defect by Cartledge and Myers<sup>15</sup> was a man (II B 4-3) whom they believed to be an offspring of the second marriage of the father (I B 1-1), who came to this country in the last third of the eighteenth century. However, we have conclusively found that II B 4-3 was in fact a son of the first marriage and that only the offspring and descendants of this marriage were affected, which would indicate that the blistering was not brought into the family by the male ancestry. In addition, it was found that illegitimate children (II B 6) of the father (I B 1-1) were not bothered with the bullous disease. His first wife (I B 2) was therefore suspected of blistering since all of her children, and only her children, blistered, as did many of her descendants. Considering this and their surnames, it would seem likely that the family (I B 2) was related by blood to the second family (I A 1). Mansur started his pedigree with a great grandmother (IV B 18), whom we found to be a great granddaughter of the man designated as (I B 1-1). It was through

this family triup that we were able to connect the pedigrees of Cartledge and Myers<sup>15</sup> to that of Mansui<sup>13</sup>

Family B represents 356 persons. Some of the sibships have been reported in material which has been published previously. Cartledge and Myers<sup>15</sup> reported the following sibships: 16, 24, 26, 27, 28, 31, 34, 38, 39, 40, 41, 42, 43, 44, 50, 51, 54, 63, 64, 65, 66, 67, and 73. They showed the following sibships incompletely, or with discrepancy from ours: 1, 2, 4, 5, 6, 7, 17, 30, 49, 70, 71, 72, 74, and 75. In Mansui's paper the following sibships have been completely shown: 56, 83, 84, 85, 95, 97, 100, 101, 102, 106, 107, 108, and 109. The following sibships were incompletely shown, or show some discrepancy from ours: 18, 79, 80, and 81. This study yields the following fifty-four additional sibships: 3, 8, 9, 10, 11, 12, 13, 14, 15, 19, 20, 21, 22, 23, 25, 29, 32, 33, 36, 37, 45, 46, 47, 48, 53, 55, 57, 58, 59, 60, 61, 62, 68, 69, 76, 77, 78, 82, 86, 87, 88, 89, 90, 91, 92, 93, 94, 96, 98, 99, 103, 104, 105, and 106.

There are 56 affected men and 62 affected women with the sex of 7 of the affected persons not known. The condition could not be determined in 35 offspring of affected parents. The children of defective parents include 123 affected, 93 normal and 35 questionably affected.

Combining families A and B, we find that in 461 persons there were 66 males and 72 females affected. Of 7 affected persons the sex was unknown. The children of defective parents include 142 affected, 115 normal and 74 of questionable status.

When the material in figures 2 and 3 is tested by the chi-square method for statistical deviation from the normal in the sex ratio of the affected persons, the raw material being taken from all the sibships which could be considered susceptible to the trait (i.e. all sibships having one affected parent), chi-square is 0.260, an insignificant deviation. This rules out sex linkage or limitation. When this material is tested for statistical deviation from the normal in ratio of affected to normal persons, the raw material for the test being taken only from susceptible sibships in which the condition of all the sibs was known to us (eliminating any sibships in which there were early deaths, premature births, stillbirths or persons of unknown condition), chi-square equals 0.268, again an insignificant deviation.

Since Greenberg<sup>4</sup> found that all his patients inherited the condition from the mother, we have tested our material from figures 2 and 3 by the chi-square method to see whether there is any evidence of either sex being the commoner transmitter. We found that the defect was transmitted by 30 mothers and 23 fathers, with a chi-square of 0.924, which shows an insignificant deviation from the expected 1:1 ratio.

In our experience men did not have bullae as frequently as women, the ratio being 10 to 109.

Epidermolysis bullosa of all types seems to be a much more frequent disease than is commonly believed. However, papers and society transactions dealing with the simple type limited to the hands and the feet have not been numerous, there being only 14 in the 213 that we reviewed. In no instance could we find as large a pedigree as we have presented in figure 3, in which there are data for 356 persons and of whom 125 are affected. Cantledge and Myers<sup>15</sup> reported 40 affected persons and Mansur<sup>13</sup> 30.

#### SUMMARY

The literature concerning epidermolysis bullosa hereditaria involving only the hands and the feet without scarring and other cutaneous changes is reviewed.

A case of epidermolysis bullosa with a family pedigree of 105 persons, of whom 10 men and 10 women suffered from the bullae of the hands and the feet, is reported (fig. 2).

The pedigrees of Mansur<sup>13</sup> and of Cantledge and Myers<sup>15</sup> are linked together, and 54 sibships are added, making a total of 109 sibships covering 356 persons, in which there are 56 affected men and 62 affected women, with the sex of 7 persons not being known. The probability of connection between families A and B is shown.

The genetic distinctiveness of different types of epidermolysis bullosa hereditaria as characterized by location of bullae on the body is pointed out.

A statistical study shows that neither the ratio of normal to affected progeny of an affected parent nor the sex ratio of affected offspring nor the ratio of male to female parent is of significant deviation from the expected 1:1, proving that we are dealing with a simple mendelian dominant trait.

A plea against the use in the title of the names of either Weber or Cockayne for a disease which neither described is made. If a proper name is to be used in describing epidermolysis bullosa hereditaria of the simple type carried by a dominant gene limited to the hands and the feet, we suggest that of Elliot's.

A new method of plotting family pedigrees is used.

# INTRAHEPATIC OBSTRUCTIVE JAUNDICE DUE TO NEOARSPHENAMINE

## Ineffectiveness of Therapy

FRED L. HARTMANN, M.D.  
AND  
ARTHUR G. SINGER, Jr., M.D.  
PHILADELPHIA

RECENTLY Freis and Matei<sup>1</sup> reported a case of jaundice due to intrahepatic obstruction consequent to the use of oxophenarsine hydrochloride. Some years previously Hanger and Gutman<sup>2</sup> collected a series of 12 cases of such a disease following the use of arsphenamine. They described the clinical and pathologic aspects of these cases and contrasted the observations with those of cases in which the jaundice resulted from parenchymatous hepatic damage. The following case is believed to belong in the first of these two groups. The disease followed the use of neoarsphenamine. The case is of interest because of the lengthy duration of the jaundice, the fact that operation was not requested, and the ultimate rapid improvement with no treatment after the failure of prolonged and varied therapy in the hospital.

### REPORT OF A CASE

A healthy 26 year old Negro, a stevedore, applied for antisyphilitic treatment in April 1944. He stated that two or three months previously he had received five intravenous injections of a yellow material from a physician in his neighborhood. There was no history of a primary or secondary syphilis, and his past history showed no serious illnesses, except an appendectomy with drainage in 1932 and gonorrhea at the age of 16. Physical examination in April 1944 revealed entirely normal conditions. The patient was well developed and well muscled and weighed approximately 170 pounds (77.1 Kg). The Wassermann and Kline reactions were strongly positive. A provisional diagnosis of latent syphilis, probably late, was made. Treatment was begun with weekly injections of 0.2 Gm of bismuth subsalicylate in oil for six weeks. Neoarsphenamine was then given, the first dose being 0.45 Gm and the next two 0.6 Gm each. There was no reaction to the first or second injection of neoarsphenamine.

From the Medical Service A, Lankenau Hospital

1 Freis, E. D., and Mater, D. A. Intrahepatic Obstructive Jaundice Following Mapharsen, with Development of a Spruelike Syndrome, *J. A. M. A.* **126** 892 (Dec. 2) 1944.

2 Hanger, F. M., and Gutman, A. B. Postarsphenamine Jaundice Apparently Due to Obstruction of Intrahepatic Biliary Tract, *J. A. M. A.* **115** 265 (July 27) 1940.



A few hours following the third injection, on June 2, the patient became nauseated, vomited repeatedly, felt weak and had a severe frontal headache. He also noted epigastric pain radiating upward along the sternum. Itching of ears and feet and dark red-brown color of his urine were observed shortly after the onset, and for several days he was unable to retain food taken by mouth. Accordingly, he was admitted to the hospital from June 7 to June 11, during which time he improved rapidly with symptomatic treatment and intravenous injection of 5 per cent dextrose in distilled water. Scleral jaundice was noted June 9, on which day there was also bile in the urine for the first time. The liver was not palpable at any time. The conditions observed on physical examination were otherwise unchanged. Laboratory studies showed hemoglobin content, 88 per cent, red blood cells, 4,240,000 and white blood cells, 10,900, of which 72 per cent were neutrophils and 28 per cent lymphocytes. The urine was entirely normal on June 7. A faint trace of albumin appeared on June 8 and June 9. Bile was found on June 9. All microscopic observations were normal. The icteric index on June 9 was 26, and the prothrombin time was 100 per cent. During this period temperature, pulse and respirations were normal.

The patient was observed on an ambulatory status during the remainder of June and part of July. He felt well during this time, but the urine continued dark and the stools were light brown. Scleral jaundice was apparent, however, and on July 12 the icteric index was 100. The patient was again hospitalized, from July 12 through July 31. Questioning revealed intolerance to eggs, pork and cabbage since his previous admission and some generalized itching. Physical examination again gave no remarkable results, except pronounced scleral jaundice. The liver was still not palpable. Laboratory studies showed no change in the blood count. The urine continued to show bile and a trace of albumin, and granular casts were reported. The urea nitrogen level of the blood was 8 mg, the cholesterol level 227 mg, the serum proteins 7.81 Gm per hundred cubic centimeters, and the prothrombin time was 100 per cent on two occasions. The icteric index rose gradually to 120. The cephalin flocculation reaction was 2 plus and the galactose tolerance test showed a total excretion of 0.9 Gm in five hours. The sulfobromophthalein sodium excretion test was unsatisfactory because of the jaundice. Roentgenograms showed a normal chest and, after ingestion of barium sulfate, a normal stomach and duodenum. Biliary drainage was unsatisfactory.

There was no change in the condition of the patient in spite of daily intravenous infusions of 10 per cent dextrose in distilled water and a diet high in carbohydrates and protein and low in fat.

From July 31 through Sept 7, 1944, the patient was followed in the outpatient department. During this time he had increased generalized itching, especially of the face and feet. In addition he continued to lose weight gradually until he was down to 145 pounds (65.8 Kg), and a persistent annoying diarrhea developed, with four to six movements a day. The diarrhea was not relieved by the usual remedies. According to the patient the stools contained pigment, and his urine continued dark. At times he felt a little dizzy, and he constantly had a bitter taste in his mouth. By August 25 the icteric index was 200, and on September 8 the patient was again hospitalized. The principal abnormality at this time was the profound jaundice visible in the scleras and the soft palate. On September 16 the liver was palpable on deep inspiration. The edge was sharp and definitely tender.

Results of laboratory studies during this admission (September 8 to November 11) were as follows. The urine continued to show no urobilinogen, but it gave a strongly positive reaction for bile constantly and showed a faint trace of albumin.

on repeated examinations. The hemoglobin was constant at 88 per cent, the red blood cells varied from 4,200,000 minimum to 4,880,000 maximum, and the white blood cells ranged from 6,100 to 10,700, with normal differential counts. The icteric index fluctuated considerably, but there was no positive trend, as shown by these values: September 12, 152, September 20, 180, October 11, 150, October 17, 135, October 31, 165, November 7, 225, and November 9, 180. The van den Bergh test elicited an immediate direct positive reaction on three occasions, with quantitative values for bilirubin in the serum of 13, 14 and 18 mg per hundred cubic centimeters. The prothrombin time had fallen to 70 per cent since the last admission, but the use of vitamin K parenterally restored the figure to 100 per cent, where it remained throughout the patient's stay, even after the use of vitamin K was stopped. Serum proteins remained normal. On September 21 they were 7.6 Gm per hundred cubic centimeters, of which 5.2 Gm was albumin and 2.4 Gm were globulin. Another determination on September 26 showed values of 6.86 Gm, 3.88 Gm and 2.88 Gm per hundred cubic centimeters respectively. The cholesterol level of the blood on September 13 was 216 mg and on November 10, 298 mg. Fractionation, however, showed that only 30 per cent of the cholesterol was in the ester form. On September 26 the alkaline phosphatase activity was 85 units, and the serum amylase 16 units.

Results of tests of hepatic function on this admission were as follows. The cephalin flocculation reaction on September 20 was 2 plus, October 18, negative and on November 10, negative. The hippuric acid synthesis test on September 16 showed 0.9 Gm excreted, on October 19, 0.9 Gm, and on November 9, 1.4 Gm. The galactose tolerance test showed 0.84 Gm excreted on September 20, and none excreted on October 17. The sulfobromophthalein sodium excretion test was again unsatisfactory because of jaundice.

Other studies showed a normal gastric acidity, failure of biliary drainage to show B bile although bile salts were reported and a flat glucose tolerance curve, with values of 81, 104, 83, 69 and 64 at 0, one-half, one, two and three hours. A roentgenologic study of the gallbladder showed failure to concentrate any of the dye given by mouth. A barium sulfate meal followed by serial roentgenologic examinations showed slow progress through the jejunum with poor peristaltic function, some distention of the loops of the intestine and increased prominence of the mucosal folds. There was no evidence of obstruction however.

Therapy used during this final period of hospitalization was directed toward protection of the liver and attempts to promote the flow of bile. Daily intravenous infusions of 1,000 cc of 10 per cent dextrose in water were given. Sorparin tablets (McNeill) (stated by the manufacturer to contain 3 grains [0.19 Gm] of extract of *Sorbus aucuparia* [mountain ash]) were given, 3 after each meal, from September 24 through October 18. Beginning October 11 sodium dehydrocholate was added to the daily infusion, 10 cc of 20 per cent solution being used. On the same day the patient received intravenously 10 Gm of methionine in the infusion.<sup>3</sup> On each day subsequently 3 Gm of methionine in water was given twice a day by mouth. This therapy was continued until the final discharge, on Nov 11, 1944. Throughout the patient's stay a diet high in carbohydrates and protein was given.

*Results of Therapy*—So far as could be observed none of the therapy described produced any definite improvement. The patient gained no weight. The icteric index showed no improvement, neither did the test of the hepatic function which was impaired (hippuric acid synthesis). There was symptomatic improvement of the itching and diarrhea. These were somewhat alleviated after admission and

gradually disappeared. The sodium dehydrocholate and methionine used did not cause any untoward effects, except for a single instance of nausea three days after their use was begun.

Following the patient's discharge on Nov. 11, 1944, there was immediate improvement, which continued steadily. He gained weight at the rate of 2 pounds (1 Kg) a week, until the total gain was 30 pounds (13.6 Kg) by February 1945. The icteric index fell each week, as shown by these values: November 9, 180, November 20, 120, November 28, 80, December 4, 70, December 11, 55, December 18, 45, December 26, 25, January 15, 1945, 15, May 7, 10. The patient felt well and soon returned to work. A final check of hepatic function was made at the end of January 1945, with these results: The cephalin flocculation reaction was negative, the hippuric acid synthesis test showed 3.9 Gm excreted, and the galactose tolerance test, none excreted. The sulfobromophthalein sodium excretion test showed a very faint trace of the dye at ten minutes and none at twenty minutes, the prothrombin time was 100 per cent.

#### COMMENT

The facts observed in this case agree largely with the observations of Hanger and Gutman in their cases of intrahepatic obstruction. The onset occurred after the third dose in a series and showed an acute constitutional reaction with gastrointestinal symptoms predominating. There was prolonged painless jaundice with severe pruritus and loss of weight. For a prolonged period the bile was diminished in the stools and increased in the urine. The cephalin flocculation reaction was not greatly altered from the normal negative, and the tolerance for galactose was not impaired. The cholesterol level of the blood was definitely increased, and the ester fraction was lowered. The urea nitrogen of the blood remained normal.

However, the alkaline phosphatase value was not elevated, there was no apparent change in the serum protein or albumin-globulin ratio, and the hippuric acid synthesis was impaired on three determinations. These observations are in disagreement with those of Hanger and Gutman.

The use of methionine in this case was based on reports of Peters and his associates<sup>3</sup> and Beattie and Marshall.<sup>4</sup> These men reported that the use of methionine prevented or minimized damage to the liver during arsenical therapy and shortened the clinical course in cases of jaundice. Peters and his associates summarized their results and concluded "that both cysteine and methionine had a significant but not remarkable effect on the course of the jaundice."

The failure of methionine and other forms of therapy to change the clinical course in the case reported here probably results from the basic

<sup>3</sup> Peters, R. A. and others. Sulphur-Containing Amino-Acids and Jaundice, *Nature*, London **153**: 773 (June 24) 1944.

<sup>4</sup> Beattie, J., and Marshall, J. Methionine in the Treatment of Liver Damage, *Nature*, London **153**: 525 (April 29) 1944.

pathologic condition present, i. e., the blockage of the tiny bile canaliculi rather than actual damage to the parenchyma of the liver itself. The conclusion drawn is that this disease described by Hanger and Gutman runs a prolonged self-limited course, unaffected by the therapeutic measures used and that time is the essential requisite for restoration to normal. Granted that the therapy may have been helpful in preserving the patient throughout his illness, there was no evidence of any specific action on the underlying pathologic changes.

#### SUMMARY

A case of prolonged, profound jaundice following the use of neoarsphenamine has been presented. The clinical and laboratory observations were those described in cases of jaundice due to obstruction of the bile canaliculi. Prolonged intensive therapy, including the use of methionine, produced no demonstrable improvement. The patient ultimately made a spontaneous complete recovery, following cessation of all therapy.

# TREATMENT OF CONGENITAL AND OF ACQUIRED SYPHILIS IN INFANTS AND IN CHILDREN BY PENICILLIN

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FOR the past two years syphilis in adults has been treated with penicillin, and at the present time it is thought that this form of therapy has been encouragingly successful. Sixteen months ago, several of us became interested in the possibility of treating babies and children with congenital and with acquired syphilis with penicillin. As penicillin is less toxic than arsenicals and heavy metals, it was felt that an effort should be made to determine whether its therapeutic efficiency was comparable to that of arsenicals and heavy metals.

In the past sixteen months, we have treated 39 syphilitic children with penicillin. Eleven of these had acquired syphilis, and 28 had congenital syphilis. There has been 1 death in our series and 3 mild reactions. We do not as yet have any idea of the optimal dosage of penicillin in the treatment of syphilis. We have used total dosages of from 500,000 units to 4,800,000 units. However, as recent articles in *The Journal of the American Medical Association*<sup>1</sup> have pointed out,

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This work was done in cooperation with the Pediatric Departments of the Washington University School of Medicine and the St Louis City Hospital. Serologic studies were done at the Snodgrass Laboratory division of the St Louis City Hospital.

The majority of the patients were treated at the Midwestern Medical Center, United States Public Health Service Rapid Treatment Hospital, St Louis.

1 Platou, R V, Hill, A J, Ingraham, N R, Goodwin, M S, Wilkinson, E E, and Hausen, A E. Penicillin in the Treatment of Infantile Congenital Syphilis, *J A M A* 127:582 (March 10) 1945.

probably the larger doses are more efficacious. The average dose for adults has been 1,200,000 or 2,400,000 units, and the latter has seemed the better. Our average dose for children now is 1,200,000 units, and if the weight dose relationship of children is comparable to that of adults certainly the children are receiving many times the average adult dose.

## I DIAGNOSIS

### 21 Cases of Congenital Syphilis

#### 7 Cases of Acquired Syphilis

The patients with congenital syphilis varied in age between 2½ months and 9 years. The larger proportion were less than 1 year of age. Those with acquired syphilis varied from 5½ months to 10 years of age. All were previously untreated.

Thirteen of the patients with congenital syphilis were in the infectious stage. In 5 of these 13 spirochetes were observed on dark field examination. In all cases a diagnosis of syphilis in the mother was established. For the other 8 patients with congenital syphilis, a diagnosis was established by serologic changes, roentgenologic evidence of osseous syphilis and other stigmas in addition to the establishment of the diagnosis of syphilis in the mother.

For the 7 patients with acquired syphilis, the diagnosis was established by the presence of positive dark field-condylomas in 3 cases, typical chancre in 1 case, morphologically typical secondary lesions in 2 cases (in 1 of which spirochetes were found on dark field examination) and a valid history and serologic reactions in the seventh case.

Eleven of the 39 patients have been treated so recently that we are not reporting on them at this time. Our reportable series, therefore, consists of 28 cases which have been followed for a minimum of two months after treatment. Data for this series of cases is presented in table 1.

## II DOSAGE

Early investigators on this problem used as a base line a total dose of 20,000 units of penicillin per kilogram of body weight. This corresponded to a 1,200,000 unit total dose for an adult. Platou, Hill, Ingraham and their co-workers employed a total of 16,000 to 32,000 units per kilogram body weight. Even more recently a medical directive issued March 24, 1945 by the Venereal Disease Division, United States Public Health Service, recommends a total dose of 40,000 units per kilogram of body weight.

Early experience led us to feel that these smaller total doses were inadequate. Our first patients were treated with a total dose of 500,000 units. Serologic response was unsatisfactory, the titer showing an

TABLE 1—Serologic Titers of Blood of Twenty-Eight Patients After Treatment at Monthly Intervals

TABLE 1—Serologic Titer of Blood of Twenty-Eight Patients After Treatment at Monthly Intervals																
Patient	Age	Diagnosis	Total Dose Penicillin Units	Serologic Titer Kahn Units												
				Initial	1 Mo	2 Mo	3 Mo	4 Mo	5 Mo	6 Mo	7 Mo	8 Mo	10 Mo	11 Mo	14 Mo	15 Mo
D S	3 mo	Cong	1,500,000	360												
J A M	2½ mo	Cong	1,700,000	360												
D M	2¼ mo	Cong	1,900,000	360												
R D	1 mo	Cong	500,000	360	120	10	80	1	1	1						
L L	1 yr	Cong	1,700,000	360	280	Lost	Lost	3	1							
R S	16 mo	Cong	1,810,000	120	360	Lost	Lost									
W J I	15 mo	Cong	1,500,000	360	10	20	10									
M F	1 mo	Cong	500,000	360	280											
R C	6 wk	Cong	1,200,000	360	120	10	Lost									
W G	2 yr	Cong	1,200,000	360	10	10	10									
R W	3 mo	Cong	1,200,000	360	120											
B F M	1 mo	Cong	1,200,000	360	10	10	40									
R H	19 mo	Cong	1,200,000	360	120	40	3	3	80	2	Neg					
E P	5 mo	Cong	1,200,000	360	120	40	3	1	10							
S R	1½ yr	Acq	1,200,000	3	1	2										
L O	5½ yr	Acq	1,000,000	1	360	240	80	1								
W A F	1 yr	Acq E Lat	1,500,000	80	80	Neg	20									
R D B	1 day	Acq	800,000	120	10	1	1	Neg	Neg							
L B	9 mo	Cong	720,000	200	120	120										
J W	10 mo	Cong	2,400,000	160	120	120										
S T	5 mo	Cong	1,800,000	80	120	120										
S W	1 yr	Cong	1,200,000	80	120	120										
D W	22 mo	Cong	1,500,000	720	120	120										
G M	10 yr	Acq	1,200,000	320	640	160										
B A	7½ mo	Cong	1,800,000	210	200	200										
M W	4½ yr	Acq	1,200,000	200	160	10										
V W	28 mo	Acq	1,200,000	160	10	10										
J B	32 mo	Cong	1,200,000	320	160	10										
			280	Pos	Pos	Pos										
* Doubtful Wassermann reaction																
† Negative Wassermann reaction																

\* Doubtful Wassermann reaction  
† Negative Wassermann reaction

initial rapid drop followed by a great increase in ten days and remaining at a high level maintained for thirty days. We therefore administered another course of 500,000 units, with no appreciable serologic response. A third 500,000 units, however, given two months after the initial therapy, was followed by a complete reversal of the serologic response. This patient had a diagnosis of florid secondary syphilis. A second case was similar in serologic response and type of treatment. Accordingly, our total dose has ranged from 80,000 to 300,000 units per kilogram of body weight, the majority of the children receiving an average dose of 100,000 to 125,000 units per kilogram. Time alone will decide whether these larger doses are more effective than the smaller doses hitherto used.

*Time Interval*—Cooke and Goldring's work has indicated that it is highly possible that the three hour time interval is too great for maximal therapeutic efficiency, inasmuch as this interval does not permit a maintenance of high constant level of penicillin in the blood stream. These authors pointed out that the highest level of penicillin in the blood is obtained from thirty minutes to one hour after injection and the level drops rapidly during the second hour with subcutaneous or intramuscular routes of administration.

In our earlier cases we felt that larger doses should have been given, but at that time penicillin was difficult to obtain and little or nothing was known as to how the drug would be tolerated in large doses by infants with syphilis.

According to Rammelkamp and Keefer<sup>2</sup> three hours has been generally conceded to be the most practical and desirable time interval between injections, in order to maintain an adequate blood penicillin level. In 3 instances, subcutaneous administration was resorted to, based on penicillin absorption curves derived by Cooke and Goldring<sup>3</sup>. Also on the basis of their work, the time interval was reduced.

The total dosage was determined by two factors: (1) available penicillin and (2) an effort to determine an effective weight dose relationship. Experimentally, in 2 cases a one hour interval was resorted to, in 1 case a two hour interval and in 1 case a four hour interval were used. In all other cases the patients were treated with a three hour interval between treatments. The individual dose varied from 10,000 (average) to 25,000 units. Some of the infants were given injections of 2,500 to 5,000 units, to minimize the possibility of a severe Herxheimer reaction.

2 Rammelkamp C. H., and Keefer, C. S. The Absorption, Excretion and Distribution of Penicillin. *J. Clin. Investigation* **22**: 425 (May) 1943.

3 Cooke, J. V. and Goldring, D. The Concentration of Penicillin in Body Fluids, *J. A. M. A.* **127**: 80 (Jan 13) 1945.



## III RESULTS

These children have been followed to date at monthly intervals whenever possible. Several of these children live in remote communities, and it has been difficult and sometimes impossible to obtain a satisfactory follow-up. The present status of the group is shown in table 1. The results are condensed in table 2.

TABLE 2—*Résumé of Results*

Lost to observation	4
Died	1
Free from syphilis (clinically and serologically)	7
With titer of less than 4 Kahn units	6
Still strongly positive for syphilis (9 with declining Kahn titer)	10
Total	28

## IV COMMENT

It is far too early to attempt any conclusive evaluation of the role of penicillin in the treatment of syphilis in children. However, certain striking effects on the child and on the disease are apparent.

1 The spirochete disappeared rapidly from local lesions, within four to eight hours no viable organisms being found.

2 The lesions healed rapidly and completely. Snuffles cleared rapidly but not as rapidly as cutaneous and mucous membrane lesions.

3 In our 3 cases, syphilitic periostitis disappeared clinically in approximately one month, and serial roentgenologic studies showed decided and progressive healing in two to three months. In three months no evidence of bony syphilis could be found.

4 Herxheimer reactions occurred in 9 instances.

5 Progressive decline in serologic titer was noted in all but 1 case in this series. In this 1 case, the titer declined at first but has remained stationary for several months. In this instance, treatment may have to be classed as failure.

6 There was a definite improvement of the child's nutritional state both during and after penicillin therapy.

7 The therapy did not interfere with the taking or retention of foods in infants.

8 In no case was infection at the site of injection observed.

9 Initial changes in the spinal fluid findings were encountered in 2 cases. In 1 of these a post-treatment spinal fluid examination was made. The serologic reaction of the spinal fluid in this case had declined from 20 to 4 Kahn units. The colloidal gold curve, total protein level and

cell counts both before and after treatment in this case were within normal limits

10 There were no evidences of a Milian reaction or secondary fever

11 In no case did we see an allergic reaction

12 One fatality occurred in this series We present herewith a summary of this case

#### REPORT OF A CASE

R DeB, a Negro girl, was admitted to St Louis Children's Hospital on Oct 17, 1944, at 24 hours of age, with chief complaints of a rash and dyspnea of eighteen hours' duration

*Family History*—The mother, aged 19, and the father, aged 21, were living and well Each gave a history of having negative Kahn reactions of the blood nine months previously Both, however, had strongly positive Kahn reactions at the time of the infant's admission

*Present Illness*—The patient was a full term baby born after a six hour labor, with spontaneous cry and respiration The cry was feeble, however, and the baby then remained quiet and seemed drowsy She was observed to breathe irregularly

*Physical Examination*—The temperature was 37 C (98.6 F) and the weight 2,850 Gm The baby was acutely ill, the cry feeble and the respirations grunting in type The mucous membranes were icteric, and the skin was covered with a purpuric eruption with areas ranging up to 1 cm in diameter and roughly circular The superficial layers of the skin were desquamating, and there was no thickening of the skin of the palms or soles The eyes showed decided icterus of the scleras There were many petechiae on the mucous membranes The chest was symmetric and the percussion note resonant bilaterally Over the bases of both lungs the breath sounds were diminished, and fine crackling rales were present Examination of the abdomen revealed a greatly enlarged spleen, which was palpable at the level of the umbilicus The Moro reflex was active The remainder of the physical examination revealed normal conditions

*Laboratory Data*—On entry the urine was normal The hemogram showed a hemoglobin level of 12.4 Gm and 35,340 leukocytes per hundred cubic centimeters with a decided left shift in the Shilling differential count A few erythroblasts and normoblasts were also present in the smear Kline, Kahn and Wassermann reactions were all positive The bleeding time was five minutes and the clotting time four and one-half minutes Clot retraction was poor in twenty-four hours

Two days later the hematology department of the Washington University School of Medicine reported on the peripheral blood as follows: red cell count, 2,150,000, hemoglobin level, 7.0 Gm, reticulocytes, 15.3 per cent, leukocytes, 16,450, and platelets, 10,750 (normal, 400,000 to 800,000) The differential count showed eosinophils, 1 per cent, myelocytes, 4 per cent, metamyelocytes, 3 per cent, band cells, 10 per cent, segmented cells, 30 per cent, lymphocytes, 40 per cent, and monocytes, 12 per cent, there were 3 normoblasts to 100 leukocytes There were decided anisocytosis and poikilocytosis This picture was thought compatible with thrombopenic purpura and chronic hemorrhage It was not compatible with erythroblastosis fetalis

An examination of the tibial bone marrow was then performed, and the observations were reported as follows: eosinophils, 8 per cent, myelocytes, 29 per cent,

myelocytes B, 8 per cent, myelocytes A, 5 per cent, metamyelocytes, 16 per cent, band forms, 16 per cent, segmented cells, 5 per cent, lymphocytes, 1 per cent, and monocytes, 0. There were 3 per cent phagocytic clasmatoocytes, 13 per cent primitive forms and 0.5 per cent reticulum cells. In counting nucleated red blood cells, in 100 leukocytes there were found 63 normoblasts, 24 late erythroblasts and 11 early erythroblasts, a total of 98. No normal mature megakaryocytes were seen. An occasional cell was seen which might have been a very young megakaryocyte. The marrow was thought to be normal but for two features. 1. There was a definite erythroid stimulation, many more normoblasts and erythroblasts being present than are seen in normal bone marrow. This was thought to be due to chronic hemorrhage. 2. The absence of normal megakaryocytes was thought to establish the diagnosis of secondary thrombopenic purpura. "The primary agent which has exerted a toxic effect on the megakaryocytes could be either (a) a toxic agent perhaps circulating in the mother's blood during her pregnancy or (b) destruction of the megakaryocytes might possibly be the result of syphilis of the bone."

Roentgenograms of long bones were reported as follows: "There is a peculiar lack of calcification at the distal ends of the shafts of all long bones of the body visualized. On the femur the area appears to be about 1.5 to 2 cm long at each end. The midportion of the shaft is of normal mineral content. The trabecular formation in the distal end appears normal. The epiphyses appear normal. Similar changes are found in the long bones of the arm and forearm on each side and in the metacarpal bones of the right hand, which can be seen on this film. The disturbance appears to be one of a diminished deposition of calcium in the growing bones during intrauterine life rather than a decalcification. This may well be the result of congenital syphilis."

Lumbar puncture ten days after entry yielded fluid which was blood-tinged and xanthochromic, and contained 12 cells. The Wassermann reaction of the spinal fluid was positive, but it was thought to be so because of the bloody tap. Eleven days later the lumbar puncture was repeated, and clear xanthochromic fluid was obtained which gave a negative Wassermann reaction.

*Course in Hospital*—The course was gradually downhill. The midline abdominal mass disappeared and was never explained. The baby did not eat well, the temperature remained normal, and anemia recurred repeatedly, it was corrected by transfusions of whole blood, only to recur. The icterus became severe, and twelve days after entry the icterus index was 250. The petechiae cleared spontaneously, and no other bleeding points were found. However, the platelet count remained low.

Penicillin therapy for congenital syphilis was begun on the baby's fourteenth day in the hospital. The drug was administered subcutaneously, 5,000 units every three hours, 720,000 units were administered prior to the baby's death, over a period of eight days. The temperature was normal the first two days, and the baby did well. On the third day the temperature spiked to 39.6 C, and from then on it continued to range between 37.5 and 40 C until death, four days later. No actual cause for the fever could be demonstrated. Cultures of blood were repeatedly sterile, and there was no leukocytosis. However, on a postmortem culture of heart blood there grew *Streptococcus viridans*. After therapy was begun, platelet counts were made each day grossly by counting the number in 100 leukocytes. They increased from 50 in 100 leukocytes to 450 in 100 leukocytes. Twenty-four hours prior to the baby's death, a mass appeared in the right lower quadrant of the abdomen, but the nature of the mass was not determined. Stools remained normal, and there was no vomiting. Abdominal distention occurred, and a few

hours later, following a feeding, the baby vomited, apparently aspirated vomitus and, despite artificial respiration and other emergency procedures, died. It was impossible to obtain permission for postmortem examination.

*Diagnoses*—The diagnoses were (1) congenital syphilis, (2) toxic thrombocytopenic purpura, possibly due to syphilis, (3) question of delayed Herxheimer reaction, and (4) question of septicemia due to *Streptococcus viridans*.

It is difficult to evaluate this case or to state positively whether death could in any way be ascribed to the antisyphilitic therapy with penicillin.

#### SUMMARY

1 Thirty-nine children and infants with syphilis have been treated with penicillin.

2 Twenty-eight cases have been followed from two to sixteen months.

3 Seven patients are clinically and serologically free from syphilis.

4 Six patients are clinically free from syphilis and serologically show a titer of less than 4 Kahn units.

5 Ten patients have strongly positive serologic reactions, but 9 of those show a declining serologic titer of the blood. These 9 patients have shown clinical improvement.

6 One patient has shown no improvement in blood serologic titer for three months.

7 One death occurred during penicillin therapy.

# OPTIMAL ZONE REACTION IN THE DIAGNOSIS AND TREATMENT OF SYPHILIS

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A PRELIMINARY report is herewith presented of a supplementary serologic procedure to serodiagnostic tests. This procedure, referred to as optimal zone procedure, is applicable to known cases of syphilis. When applied to such cases, it gives promise to be of value (1) in supporting the diagnosis of clinically positive, seronegative syphilis, (2) in providing an index of cure in syphilis more dependable than serodiagnostic tests, especially in evaluating rapid methods of treatment, and (3) in demonstrating different precipitation patterns in different situations in syphilis patterns which give indication of having clinical significance.

## 1 BASIS OF OPTIMAL ZONE PROCEDURE

The optimal zone procedure is based on an extension of the serum antigen ratios from three, employed in the standard Kahn test, to ten and, in some cases, fifteen ratios. Twenty years ago,<sup>1</sup> when my interest was directed to the principles governing the phenomenon of precipitation in syphilis which laid the foundation for the standard Kahn test, I reported that for optimal precipitation results it is necessary to employ appropriate serum antigen ratios. I then employed a range of serum antigen ratios of 1:2, 1:1, 1:5, 1:2, 1:3, 1:6, 1:12, 1:24 and 1:1 and observed that the stronger the reacting capacity of the serum the greater the tendency toward positivity with increasing amounts of antigen while the weaker the reacting capacity of the serum the greater the tendency toward positivity with decreasing amounts of antigen. This observation led me at first to consider the use of six or more serum antigen ratios for a serodiagnostic test, but for reasons of greater practicability in routine blood testing the use of three serum antigen ratios, namely 1:3, 1:6 and 1:12, was decided on. These three ratios, employed in the standard Kahn test, strike a good average of serologic reactivity for a serodiagnostic test in the majority of

From Clinical Laboratories, University Hospital, University of Michigan

1 Kahn, R. L. (a) Serum Diagnosis of Syphilis by Precipitation, Baltimore, Williams & Wilkins Company, 1925, p. 54, (b) The Kahn Test A Practical Guide, *ibid*, 1928, p. 17

cases of syphilis, but to determine optimal serologic reactivity in certain cases an extension of these ratios is necessary

The relationship between the standard Kahn and optimal zone technics is presented in table 1. Ten serum:antigen ratios are employed, namely 1:1, 2:1, 3:1, 6:1, 12:1, 24:1, 36:1, 48:1, 76:1 and 100:1. For simplicity, these ratios are divided into three zones. Zone II represents the ratios employed in the standard Kahn test, zone I consists of ratios in which the antigen is increased in relation to the serum, and zone III consists of ratios in which the serum is increased in relation to the antigen. The precipitation results are recorded as negative (-), doubtful ( $\pm$ ), 1 plus (1), 2 plus (2), 3 plus (3), 4 plus (4), depending on the degree of precipitation.

TABLE 1—*Illustrative Patterns of Optimal Zone Reaction*

Serologic Pattern Number	Serum:Antigen Suspension									
	Zone I			Zone II (Standard Kahn)			Zone III			
	1:1	2:1	3:1	6:1	12:1	24:1	36:1	48:1	76:1	100:1
Optimal Precipitation with Increase of Antigen over Serum										
1	4	4	1	—	—	—	—	—	—	—
	4	4	4	4	4	4	1	—	—	—
	4	4	4	4	4	4	4	1	—	—
Optimal Precipitation with Moderate Amounts of Serum and Antigen										
2	—	—	—	1	4	2	1	—	—	—
	—	—	1	4	4	4	1	—	—	—
	—	1	4	4	4	4	4	1	—	—
Optimal Precipitation with Increase of Serum over Antigen										
3	—	—	—	—	—	—	—	4	4	4
	—	—	—	—	1	4	4	4	4	4
	—	—	4	4	4	4	4	4	4	4
Precipitation in All Ratios										
4	4	4	4	4	4	4	4	4	4	4
Negative in All Ratios										
5	—	—	—	—	—	—	—	—	—	—

Four serologic patterns are illustrated in the table. In pattern 1, optimal precipitation is noted in zone I, in which the antigen is increased in relation to the serum. In pattern 2, optimal precipitation is noted in zone II or on the borders of zones II and III, in which the amounts of antigen and serum are not noticeably increased over one another. In pattern 3, optimal precipitation is noted in zone III, in which the serum is increased over the antigen. In pattern 4, precipitation is noted in all ratios.

2. OPTIMAL ZONE REACTION IN SUPPORTING THE DIAGNOSIS OF CLINICALLY POSITIVE SERONEGATIVE SYPHILIS

The occasional occurrence of seronegative reactions in the presence of syphilis has remained an anomaly in the serologic behavior of this

disease. Considering the high sensitivity of modern serodiagnostic technics, it might have been expected that seropositivity would be attained in all known cases of syphilis. Actually, seronegativity is encountered in the presence of syphilis not only with serodiagnostic tests but also with supersensitive tests, such as the Kahn presumptive and Kline exclusion technics. "Seronegative syphilis" has indeed become a commonplace term in clinical medicine, and clinicians and serologists have long emphasized that a negative reaction to serodiagnostic tests does not eliminate the possibility of syphilitic infection. What is particularly anomalous is the fact that the same serodiagnostic tests which elicit negative reactions in certain known cases of syphilis elicit positive reactions in certain cases in the absence of this disease,

TABLE 2—*Cases of Syphilis Showing Optimal Precipitation in Zone I or III and not in the Serum Antigen Range of the Standard Kahn Test*

Case No	Serum Antigen Suspension										Clinical History of Syphilis
	Zone I		Zone II (Standard Kahn)			Zone III					
	1:1	2:1	1:1	6:1	12:1	24:1	48:1	76:1	100:1		
1	—	—	—	—	1	4	4	4	4	4	Primary
2	—	—	—	—	—	4	4	2	1	1	Primary
3	—	—	—	—	—	—	2	±	—	—	Primary
4	—	—	—	—	—	4	4	4	—	—	Early latent
5	—	—	—	—	—	4	4	4	2	1	Early latent
6	4	—	1	—	—	—	—	—	—	—	Congenital
7	4	4	±	—	—	—	—	—	—	—	Congenital
8	4	4	2	—	—	—	—	—	—	—	Congenital
9	4	4	1	—	—	—	—	—	—	—	Neurosyphilis
10	4	4	—	—	—	—	—	—	—	—	Neurosyphilis

for it would seem reasonable to believe that serodiagnostic tests so sensitive as to give "false positive" reactions would be free from "false negative" reactions.

Among the explanations generally offered for seronegativity in cases of syphilis are that the host is incapable of producing antibodies, that the blood serum contains an inhibitory substance, and that the colloidal state of the serum masks reactivity with the antigen. Studies on optimal zones of reactivity in the serology of syphilis indicate that the occurrence of at least certain false negative reactions with modern serodiagnostic tests is due to the limited serum-antigen ratios employed in these tests. Table 2 presents data of 10 cases of syphilis in which the optimal precipitation zone is outside the serum-antigen range of the standard Kahn test. It is evident that persons with syphilis may show optimal precipitation in zone III and no precipitation in zones I and II while others may show optimal precipitation in zone I and very weak or no precipitation in zone II. Thus, in a certain percentage of cases

of syphilis negative reactions may be obtained with a serodiagnostic test, not because the patients are truly seronegative but because the serum antigen ratios employed in the test are not optimal for these patients

All serodiagnostic tests, whether precipitation or complement fixation, to my knowledge, employ single ratios of serum to antigen, with the exception of the standard Kahn test, which, as already indicated, employs three ratios. Actually, a test employing one ratio of serum to antigen can easily be as sensitive as, or more sensitive than, a test employing three ratios, all that is necessary is the use of an antigen of sufficiently high sensitivity. Thus, the presumptive Kahn procedure, which employs a single ratio of serum to antigen, is about 10 per cent more sensitive than the standard Kahn test, owing to the increased sensitivity of the antigen. As the sensitivity of the antigen is increased, the optimal zone of precipitation with different serum antigen ratios widens but the basic serologic pattern remains the same. Hence, when serodiagnostic tests or supersensitive tests elicit negative reactions in known cases of syphilis, it can mean only that the reactions are negative in the serum antigen ratios employed and it is possible that positive reactions would be obtained in other serum antigen ratios.

Based on these considerations, it becomes understandable why modern serodiagnostic tests may elicit negative reactions in certain cases of syphilis and yet elicit positive reactions in the absence of the disease. The explanation appears to be that the limited serum antigen ratios of serodiagnostic tests may not be optimal for certain cases of syphilis and may be optimal for certain nonsyphilitic cases. It is not claimed that the optimal zone procedure will elicit positive reactions in all cases of syphilis in which serodiagnostic tests elicit negative reactions. Only prolonged trial can indicate the extent to which this procedure will elicit positive reactions in such cases. That it elicits positive reactions in some of these cases is evident from the data presented in this article.

### 3 OPTIMAL ZONE REACTION IN THE ESTABLISHMENT OF CURE FOLLOWING THERAPY IN SYPHILIS

It is common knowledge that seronegativity following therapy cannot be taken as a criterion of cure. This is understandable. For as long as seronegativity is encountered in certain cases in the presence of syphilis, seronegativity following therapy might also occur in the presence of the disease. If it were possible to have a serologic procedure which would be able to detect nearly all cases of syphilis, negativity following therapy could, with reasonable certainty, be accepted as a criterion of cure. Hence, to the extent to which the optimal zone procedure will prove effective in the detection of syphilis in all its



manifestations, it will prove similarly effective as a criterion of cure following therapy

In the evaluation of the rapid methods of treatment, it would seem particularly desirable to apply the optimal zone procedure. The prolonged follow-up system necessary with the use of present day serodiagnostic tests is well known and is important as an aid in the detection of relapses. But relapses can mean only that the patients under observation have never been cured, hence, they may never have been truly seronegative. They merely became negative with serodiagnostic tests, which is equivalent to being negative in the particular serum antigen ratios employed in these tests. They might have shown positivity in certain serum antigen ratios of the optimal zone procedure.

There is obviously great need for a serologic criterion of cure in syphilis. It is clear that any such criterion will have to undergo extensive and prolonged trial. Considering, however, the time and expense necessary to follow up a patient who, let us say, had undergone one of the rapid methods of treatment, the use of an elaborate serologic method such as the optimal zone procedure seems justifiable.

#### 4. OPTIMAL ZONE REACTION IN THE DEMONSTRATION OF DIFFERENT PRECIPITATION PATTERNS IN DIFFERENT SITUATIONS IN SYPHILIS

In 1923<sup>2</sup> I reported different precipitation trends with the three serum antigen ratios of the standard Kahn test (table 3). In some

TABLE 3—*Typical Precipitation Reactions with Four Different Serums*

Serum	Serum Antigen Suspension			Clinical Diagnosis
	3 1	6 1	12 1	
1	4	4	4	Hunterian chancre, early secondary
2	4	2	—	Probably latent, untreated
3	±	2	4	Intensively treated
4	—	—	—	Free from syphilis

Adapted from Kahn<sup>2</sup>

instances complete precipitation was noted in all three ratios, in others complete precipitation was noted only in the ratio in which the serum was increased in relation to the antigen, in still others complete precipitation was noted only in the ratio in which the serum was reduced in relation to the antigen. This observation gave some indication of the existence of different serologic patterns in syphilis. To elicit these patterns fully, however, it was necessary to employ an extensive serum antigen range.

<sup>2</sup> Kahn, R. L. Rapid Precipitation Phase of the Kahn Test for Syphilis, JAMA 81:88 (July 14) 1923.

Table 4 presents the four precipitation patterns of the optimal zone reaction in 24 cases of syphilis in which the patients have undergone various degrees of therapy. Pattern 1, in which optimal precipitation occurs with excess of antigen in relation to serum (zone I), is noted most frequently in late syphilis, less frequently in early syphilis. Pattern 2, in which optimal precipitation occurs with moderate amounts of serum and antigen (zone II), is noted most frequently in cases of treated syphilis both early and late. Pattern 3, in which optimal pre-

TABLE 4—Optimal Zone Reactions in Different Cases of Syphilis

Case No	Serum     Antigen Suspension										Clinical Diagnosis of S <sub>3</sub> phills
	Zone I		Zone II (Standard Kahn)				Zone III				
	1 1	2 1	3 1	6 1	12 1	24 1	36 1	48 1	75 1	100 1	
Optimal Precipitation with Increase of Antigen over Serum											
1	4	4	4	1	—	—	—	—	—	—	Late latent
2	4	4	4	4	4	4	—	—	—	—	Late latent
3	4	4	4	4	4	2	1	—	—	—	Late latent
4	4	4	4	4	4	2	—	—	—	—	Late latent
5	4	4	4	4	4	4	4	4	—	—	Early latent
6	4	4	4	4	4	4	3	5	2	1	Secondary
Optimal Precipitation with Moderate Serum Antigen Amounts											
7	—	—	—	±	3	1	—	—	—	—	Early latent
8	—	—	—	±	3	2	2	—	—	—	Early latent
9	—	—	—	1	4	4	4	—	—	—	Late latent
10	—	—	—	2	4	4	4	3	—	—	Late latent
11	—	—	—	4	4	4	4	5	—	—	Tabes
12	—	4	4	4	4	4	4	2	1	1	Secondary
Optimal Precipitation with Increase of Serum over Antigen											
13	—	—	—	—	1	3	4	4	4	4	Primary
14	—	—	—	—	—	4	4	4	4	2	Primary
15	—	—	—	4	4	4	4	4	4	4	Primary
16	—	1	4	4	4	4	4	4	4	4	Primary
17	—	4	4	4	4	4	4	4	4	4	Secondary
18	—	—	2	4	4	4	4	4	4	4	Late latent
Precipitation in All Ratios											
19	3	4	4	4	4	4	4	4	4	4	Primary
20	4	4	4	4	4	4	4	4	4	4	Secondary
21	4	4	4	4	4	4	4	4	4	4	Secondary
22	4	4	4	4	4	4	4	4	4	4	Early latent
23	4	4	4	4	4	4	4	4	4	4	Late latent
24	4	4	4	4	4	4	4	4	4	4	General paresis

cipitation occurs with excess of serum in relation to antigen (zone III), is noted frequently in early syphilis and least frequently in late syphilis. Pattern 4, in which precipitation is noted in all serum antigen ratios, may occur apparently in all stages of syphilis, especially of untreated or of little treated syphilis.

The significance of the different precipitation patterns in the diagnosis and treatment of syphilis can be determined only if these patterns are observed in the same patients before, during and after therapy. Thus, 2 patients with the primary stage of syphilis may have positive reactions with serodiagnostic tests and precipitation readings of

-- 2 4 4 4 4 4 4 with the optimal zone procedure. In the course of several months, after having been treated by one of the rapid methods, the patients have negative reactions with serodiagnostic tests. But with the optimal zone procedure the patients show some serologic activity, patient 1 having precipitation readings of --- 1 4 3 --- and patient 2 showing readings of 4 2 --- --- ---. These precipitation readings indicate decided differences in the serologic response of these 2 patients to the therapy. Patient 1 exhibits a serologic picture common in cases of treated syphilis approaching negativity. The antibody concentration of the serum is low, and positivity can be demonstrated only in a narrow range of serum antigen ratios, apparently optimal in the middle zone. This residual positivity may spontaneously disappear in the course of a month or two, the patient becoming completely seronegative, or it may flare up as a result of a clinical relapse. Patient 2, on the other hand, exhibits a serologic picture common in late syphilis. Precipitation is noted only in the first two ratios of the optimal zone procedure, presumably because the serum is especially rich in antibodies and hence reacts only with the large amounts of antigen present in these ratios. The negative readings in the remaining eight ratios are due to the disproportionate amounts of antibodies and antigen in these ratios—namely, very high concentration of antibodies and low concentration of antigen. If the concentration of antibodies is reduced by diluting the serum with isotonic solution of sodium chloride, positive precipitation will be obtained in these ratios. Patient 2, with this serologic response, is not likely to become seronegative spontaneously, and he may indeed need extraordinary therapeutic measures. Obviously, the full significance of each of the four serologic patterns in the diagnosis and treatment of syphilis can become evident only after extensive trial.

It should be emphasized that the optimal zone procedure is not a serodiagnostic test to aid physicians in the establishment of a diagnosis of syphilis. As already pointed out, it is applicable only to cases in which a diagnosis of syphilis has already been established. Also, the optimal zone procedure is of no value in the detection of false positive reactions, for which my verification test<sup>3</sup> is employed in this laboratory. The extent to which the procedure gives different serologic patterns with various animal (pig, horse, rabbit and other) serums is under investigation in this laboratory. Thus far it has been observed that certain of these serums show precipitation in all ten serum antigen ratios and that others show optimal precipitation in zone III, in which the serum is in excess of antigen.

3 Kahn, R. L. Technique of the Standard Kahn Test and of Special Kahn Procedures, Ann Arbor, University of Michigan Press, 1946, p. 31.

## 5 QUANTITATIVE OPTIMAL ZONE REACTION

Quantitative optimal zone determinations are carried out by making serial dilutions of serum with isotonic solution of sodium chloride and employing these dilutions in each of the serum antigen ratios of the optimal zone procedure, the highest dilution of serum showing precipitation is the optimal quantitative titer. Present day quantitative serologic procedures are based on a single ratio of serum to antigen. This ratio may or may not give the optimal quantitative titer in a given case. Thus, in a syphilitic person giving an optimal zone reaction, let us say, of -- 4 4 4 2 -- --, the routine quantitative Kahn procedure, employing a 6 : 1 ratio of serum : antigen, is likely to give the optimal quantitative titer. But for a syphilitic person giving an optimal zone reaction of -- -- -- 2 4 4, the 6 : 1 serum : antigen ratio is not applicable, as it lies within the zone of seronegativity and any quantitative determination in that ratio is likely to give negative results. In this case, a quantitative test performed with a serum : antigen ratio of 76 : 1 might give the optimal quantitative titer.

In the early years of the Kahn reaction, I considered the use of three serum : antigen ratios in the diagnostic test and eight or ten ratios in the quantitative test.<sup>4</sup> Hopkins and Rockstraw<sup>5</sup> and Wilson, Kurtz and Larkum<sup>6</sup> also suggested the use of increased serum : antigen ratios over the three ratios of the diagnostic test for quantitative determinations. The main difficulty with the use of multiple serum : antigen ratios in a quantitative procedure was the requirement of a relatively large amount of serum, such as 2 cc. I chose instead a quantitative procedure, since known as the quantitative Kahn procedure, based on serial dilutions of serum with isotonic solution of sodium chloride, for which relatively minute amounts of serum, such as 0.1 or 0.2 cc., are sufficient.

It is not recommended that quantitative optimal zone determinations replace the quantitative Kahn procedure in the routine follow-up of treated patients. The simplicity of the latter procedure and its basic value in the majority of cases make it preferable for routine use. The clinical value of the quantitative optimal zone procedure is under investigation.

## 6 TECHNIC OF OPTIMAL ZONE PROCEDURE

The technic of the optimal zone procedure is outlined in table 5. It will be noted that the serum and the antigen suspension in zone II are employed in micro amounts. The antigen suspension is measured with a 0.1 cc. pipet graduated in 0.001 cc. The serum in amounts up

<sup>4</sup> Kahn,<sup>1b</sup> p. 132.

<sup>5</sup> Hopkins, J. G., and Rockstraw, E. W. Quantitative Determination of the Kahn Reaction, *J. Lab. & Clin. Med.* **13** 146 (Nov.) 1927.

<sup>6</sup> Wilson, D., Kurtz, M. B., and Larkum, N. W. The Zone of Precipitation in the Kahn Test, *Am. J. Syph. & Neurol.* **18** 355 (July) 1934.

to 0.2 cc is measured with a 0.2 cc pipet graduated in 0.001 cc, and in amounts over 0.2 cc with a 1 cc pipet graduated in 0.01 cc. The isotonic solution of sodium chloride is also measured with a 1 cc pipet, or if desired, with a 2 cc pipet. The technical steps are the same as those employed in the standard Kahn test.

The types of reactions noted are illustrated in table 1. In reporting to physicians, it seems best to report the readings in all ten tubes. Thus, when all tubes show a 4 plus precipitation, the report should read 4 4 4 4 4 4 4 4 4 4, and when none of the tubes show precipitation the report should read — — — — —. It is evident that tubes 3, 4 and 5 in the series contain the serum-antigen ratios employed in the Kahn test.

The optimal zone procedure, while consisting of ten ratios of serum-antigen, need not be limited to that number of ratios, additional

TABLE 5—*Technic of Optimal Zone Procedure*

Serum-Antigen Suspension									
Zone I		Zone II (Standard Kahn)				Zone III			
1:1	2:1	3:1	6:1	12:1	24:1	36:1	48:1	76:1	100:1
Standard Antigen Suspension, Cc									
0.05	0.05	0.02	0.01	0.01	0.01	0.005	0.005	0.005	0.005
Serum, Cc									
0.05	0.1	0.06	0.06	0.12	0.24	0.18	0.24	0.38	0.5
0.9% NaCl Solution, Cc									
1.0	1.0	0.4	0.4	0.3	0.2	0.25	0.2	0.1	0

The tubes are shaken for three minutes, and the results are read after the addition of salt solution.

ratios, such as 1:2 and 1:3 and 150:1 and 200:1, might be employed in some cases. Studies are in progress to determine the value of sensitized antigen (of the presumptive test) in the optimal zone procedure.

Indications are that only antigens having "sloping" titers are suitable in eliciting different precipitation patterns with the optimal zone reaction and that antigens having "flat" titers are not suitable. Antigens having sloping titers show titration pictures of increasing clarity with the increase in the amounts of isotonic solution of sodium chloride in the preparation of the antigen suspensions. Antigens having flat titers show titration pictures of similar clarity with the increase in the amounts of isotonic solution of sodium chloride in the preparation of the antigen suspensions. Efforts are being directed in this laboratory to standardize all Kahn antigens to exhibit sloping titers.

## 7 SUMMARY

A serologic method is presented, of a broader scope than current serodiagnostic tests, intended to supplement these tests in cases in which the diagnosis of syphilis is definitely established. This method, known as the optimal zone procedure, is based on the use of multiple serum antigen ratios. By the use of these ratios, positive results may be obtained in known cases of syphilis in which serodiagnostic tests give negative results. Also, negative results given by the procedure following therapy in syphilis may serve as a better indicator of cure than negative results given by serodiagnostic tests. Finally, the method elicits different serologic patterns in different situations in syphilis—patterns which may indicate serologic trends of clinical significance.

Clinical material for this paper was furnished by Dr. Arthur C. Curtis, acting chairman of the department of dermatology and syphilology, University Hospital, University of Michigan; by Dr. Grant Morrow, of the same department, by Major Nelson Ryan, United States Public Health Service, director, Michigan Rapid Treatment Center, Ann Arbor, and by Dr. Loren W. Shaffer, director, Social Hygiene Clinic, Detroit. Technical assistance was rendered by Ella M. Brandon, Catherine Adams and Elizabeth B. McDermott.

# Clinical Notes

## MOLLUSCUM CONTAGIOSUM TREATED WITH SULFADIAZINE

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In 1941 Sommerville<sup>1</sup> reported on 8 cases of molluscum contagiosum in which the patients had been treated with sulfapyridine. In 6 cases the disease cleared completely, and in 2 it was necessary to stop the treatment within a short time because of toxic reactions to the drug. Sommerville pointed out that sulfapyridine had a definite lethal effect on the causative virus of molluscum contagiosum. Four of Sommerville's patients who took sulfapyridine regularly in doses of 30 to 60 grains (2 to 4 Gm) daily were cured within varying periods of two to eight weeks. For 2 patients who took the drug only at irregular intervals three to four months was required for complete cure. Two patients who failed to respond when the daily dose was 15 grains (1 Gm) had clearing when the dosage was increased to 30 grains daily. Of the 6 patients who were cured, 5 were children ranging in age from 9 months to 15 years.

In 1942 Hill and Downing<sup>2</sup> reported another case of molluscum contagiosum in a white man aged 44, which responded favorably to sulfapyridine. There were fifteen lesions of one year's duration on the trunk and arms. The patient was given sulfapyridine (7½ grains [0.5 Gm] four times daily), and within a week all the lesions except one had disappeared. The latter was removed by desiccation. There were no recurrences within four months following treatment.

A few months ago I observed a case of molluscum contagiosum in a child in which the lesions were so numerous that local therapy would have been a formidable procedure. Chemotherapy with sulfadiazine was completely successful. The patient was a boy aged 12, who reported for examination on March 8, 1945. There were about a hundred lesions of molluscum contagiosum on the buttocks, in the intergluteal cleft and on the scrotum. Treatment with sulfadiazine (15 grains orally four times daily) was instituted on March 15. Within one week the lesions had diminished in size considerably. The dosage of the drug was reduced to 7½ grains four times daily, and within another week the only signs of the disease were pink macules at the sites of former nodules. There has been no recurrence in several months.

### COMMENT

From the few reports in the literature it seems that both sulfapyridine and sulfadiazine are effective drugs in the treatment of molluscum contagiosum. Other sulfonamide compounds might be similarly useful. Because of possible toxic reactions the routine use of sulfonamide compounds in treating this disease however, seems hardly justifiable, since simple harmless local measures are successful in ordinary cases. For certain persons, especially children, whose lesions are extremely numerous chemotherapy with sulfonamide compounds may be used.

From the Division of Dermatology, University of Minnesota, H. E. Michelson, M. D., Director.

1. Sommerville, J. Molluscum Contagiosum and M. & B. 693, Brit. J. Dermat. **53**: 255-257 (Aug-Sept.) 1941.

2. Hill, W. R., and Downing, J. G. Molluscum Contagiosum Cured with Sulfapyridine. Arch. Dermat. & Syph. **46**: 139-140 (July) 1942.

## PURPURA DUE TO IODIDES

### Report of a Case

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The occurrence of purpuric manifestations following the administration of iodides was recorded in 1877 by Fournier<sup>1</sup> Other reports were made by Robinson in 1893,<sup>2</sup> Milian in 1899,<sup>3</sup> Mackenzie in 1889,<sup>4</sup> Wilson in 1889,<sup>5</sup> Hudelo and Lebar in 1904<sup>6</sup> and Denning in 1933.<sup>7</sup> While cutaneous manifestations from the internal use of iodides are common, and, indeed, often anticipated, we feel that purpuric lesions are of sufficient rarity to justify this case report We consider that purpura resulting from iodides is an ominous sign—if the use of the drug is continued, a fatality might result Therefore one must recognize the possibility that purpura can be caused by the administration of iodides In our experience, it occurs so rarely as to make one suspect other causes rather than the obvious (and true) one

#### REPORT OF CASE

B F, a 48 year old man, was first seen by one of us (W C D) in November 1944 He complained of severe headaches, progressive loss of vision in the right eye and some unsteadiness of gait

Physical examination showed a positive Romberg sign and diminished knee jerks and ankle jerks The heart and lungs were normal

Ophthalmologic examination showed 20/50 vision in the left eye and 20/200 vision in the right eye The pupils were unequal and did not react to light There was pallor of the optic nerves

The Kolmer and Kahn serologic reactions of the blood were 4 plus The Kahn reaction of the spinal fluid was 4 plus, there were 87 cells per cubic millimeter, the total protein level was 80 mg per hundred cubic centimeters, and the colloidal gold curve (Lange test) was 011231000 Adagnosis of tabes dorsalis (with primary atrophy of the optic nerve) was made

On November 13 the patient was instructed to take 15 grains (1 Gm) of potassium iodide three times daily This was accompanied with weekly intramuscular injections of bismuth subsalicylate (0.2 Gm) His headaches diminished in severity, and his vision rapidly improved He reported some soreness in the salivary glands This was attributed to the potassium iodide, but he was advised to continue taking it

1 Fournier, A Petechial Iodism, *Rev mens de med et chir* **1** 653-664, 1877

2 Robinson, T Rapid Production of Purpura After Small Doses of Iodide of Potassium, *Lancet* **1** 471, 1893

3 Milian, G Iodide Purpura of the Buccal Mucosa, *Presse med* **2** 193, 1899

4 Mackenzie, S Fatal Purpura From Iodide of Potassium, *Illus M News* **1** 169, 1888-1889

5 Wilson, J H Purpura Haemorrhagica from Iodide of Potassium, *Brit M J* **1** 470, 1889

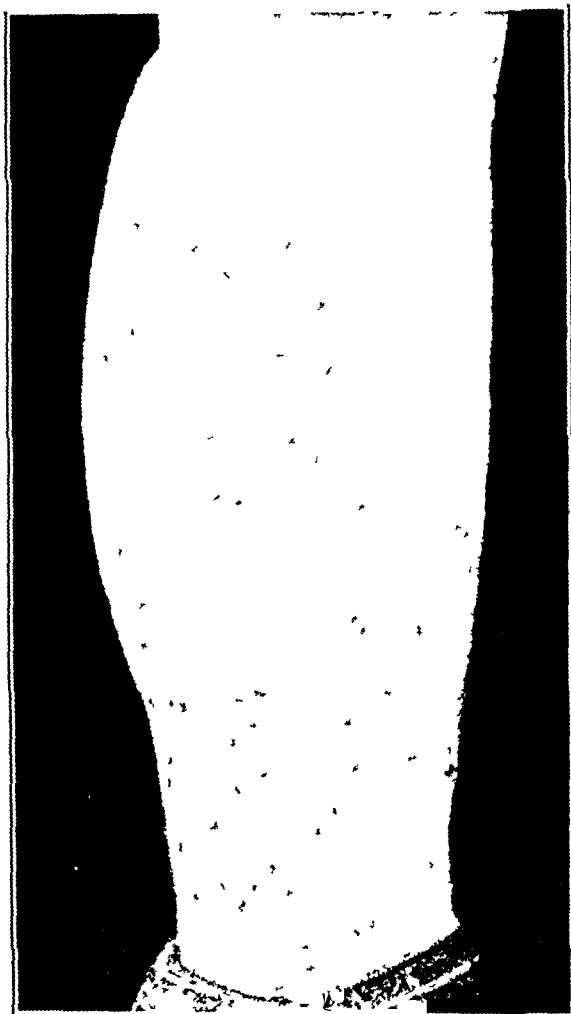
6 Hudelo and Lebar Purpuric Iodism with Probable Association of Tubercules of the Angiokeratoma Variety, *Bull Soc franç de dermat et syph* **15** 361-364, 1904

7 Denning, H Thrombopenic Purpura Following Medication with Iodine, *Munchen med Wchnschr* **80** 562, 1933



On December 1 definite purpura of the lower extremities was noticed by the patient and the physician. No other signs or symptoms were present. Examination of the blood at this time showed a hemoglobin content of 86 per cent (Sahli), 4,560,000 red cells, 12,400 white cells and 100,000 platelets.

Feeling that the bismuth was responsible for the purpura, we discontinued its use and administered oxophenarsine hydrochloride. However, the purpura persisted. Our attention was now drawn to the potassium iodide as a possible cause, hence



Purpuric lesions produced by readministration of potassium iodide

it was discontinued. The purpuric lesions promptly disappeared. Since they cleared, we have been able to reproduce the lesion experimentally by a single dose of 5 grains (0.3 Gm.) of potassium iodide (fig.)

#### SUMMARY

A case of purpura from the administration of potassium iodide is reported. Because of its ominous import, we feel that the possibility of the production of purpura should be kept in mind whenever iodides are used.

Medical-Dental Building

Medical Arts Building

# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

ACUTE SYPHILITIC MENINGITIS TREATED WITH PENICILLIN RUSSELL A NELSON  
and LEROY DUNCAN, Am J Syph, Gonorr & Ven Dis 29 141 (March) 1945

In 10 cases of acute syphilitic meningitis treated with penicillin intramuscularly, the immediate results were excellent, from both the clinical and the laboratory standpoint. While penicillin does not appear in the cerebrospinal fluid after frequent intramuscular administrations, the drug is effective against acute syphilitic meningitis when given by the intramuscular route.

Clinical relapse did not develop in any of the 10 patients treated (ninety-eight to three hundred and ten days after treatment). One patient showed a serologic relapse in the spinal fluid.

The total amount of penicillin administered to a patient varied from 600,000 to 4,000,000 units, the duration of treatment varied from seven and one-half to eleven days.

The authors recommend that patients with acute syphilitic meningitis receive a total of 2,000,000 to 3,000,000 Oxford units of penicillin administered by the intramuscular route every three to four hours day and night over a minimum period of eight to sixteen days.

FALSE POSITIVE SEROLOGIC REACTIONS FOR SYPHILIS WITH SPECIAL REFERENCE  
TO THOSE DUE TO SMALLPOX VACCINATIONS (VACCINIA) R REIN and  
ELIZABETH S ELSBERG, Am J Syph, Gonorr & Ven Dis 29 303 (May) 1945

Biologic false positive reactions occur with some frequency following vaccinations for smallpox, and it is important to rule out that possibility before anti-syphilitic treatment is instituted. From the results obtained in this study it would seem that about ten to fourteen days must elapse after vaccination for smallpox before the first false positive reaction for syphilis is detected. A similar incubation period was noted in patients with primary atypical pneumonia, while in malaria false positive reactions are observed four to seven days after the first febrile attack.

Following vaccination the maximum degree of positivity was usually seen between the fourteenth and the twenty-first day. The majority of serums with false positive reactions due to smallpox vaccination became negative within three months.

PENICILLIN IN LATE SYPHILIS J H STOKES and others, Am J Syph, Gonorr & Ven Dis 29 313 (May) 1945

The authors by means of tables and case records attempt to evaluate the status of penicillin in treatment of late syphilis. Striking improvements were obtained in syphilis of the central nervous system and in late cutaneous syphilis. Interstitial keratitis showed an erratic response to penicillin, and the response of serofastness in late latent syphilis is not encouraging thus far.

As a general statement it may be said that penicillin, as the sodium salt of an as yet incompletely analyzed and understood substance, is an effective therapeutic agent in the treatment of late syphilis. Under conditions not yet clearly defined, it produces transformations, symptomatically and serologically, without reaction or even serious inconvenience to the patient, which are equal if not superior to those obtained by long and arduous procedures involving the arsenicals and heavy metals.

TIME-DOSE RELATIONSHIPS OF PENICILLIN THERAPY W McDERMOTT, MARIA BENOIT and R DuBOIS, *Am J Syph, Gonorr & Ven Dis* **29**.345, 1945

Observations of the action of penicillin on infectious syphilis suggest that only short periods of action of penicillin are necessary for the immediate destruction of a large number of organisms but prolonged action is necessary for cure. In addition, there is some evidence that in vivo large increases in the concentration of penicillin for short periods do not shorten the period of time necessary for cure.

As both studies in vitro and clinical experience lend support to the thesis that it is not the production of multiple peaks of high concentrations of penicillin but the length of the action at low concentrations which is the important factor, it is suggested that the action time of penicillin be given consideration in the planning of new regimens for the treatment of syphilis.

There is a possibility that once the initial effect of the penicillin action has occurred subsequent action need not be absolutely continuous to obtain the maximum effect.

REUTER, Milwaukee

TREATMENT OF SKIN DISEASES IN THE TROPICS THOMAS W CLARK, *Bull U S Army M Dept*, April 1945, no 87, p 70

The cutaneous diseases most commonly encountered in an Army hospital served for more than a year and a half in the South and Southwest Pacific were dermatophytosis, dermatitis venenata and bites of insects and mites. The characteristics of these diseases were much the same as in temperate zones, but they tended to be more persistent and severer. Secondary infections complicated nearly every case, and most often it was the infection, and not the primary disease, that led to hospitalization.

Good general care, strict adherence to aseptic surgical technics and the judicious use of local therapy were the important factors in the treatment.

CONTACT POISON PLANTS IN THE OLD WORLD TROPICS E D MERRILL, *Bull U S Army M Dept*, April 1945, no 87, p 115

Many physicians perhaps do not realize that certain trees and some shrubs in the Old World tropics, all belonging in the same natural family of plants as the poison oak and poison ivy (*Rhus*), the Anacardiaceae, are violent contact irritants. Contact with the fresh sap, and some species with fresh leaves, or with freshly sawed lumber may cause violent dermatitis corresponding exactly to that caused by *Rhus*. The genus *Rhus* is of worldwide distribution and contains about two hundred described species, yet only a very few of the species are actually poisonous, these are confined to North America, eastern Asia and Japan. In the Indo-Malaysian region some of the species in certain other anacardiaceous genera are poisonous, all of these, with the exception of some shrubs of genus *Semecarpus*, are trees.

As in certain persons a characteristic eruption, known as mango rash, develops after the eating of the fruits of the common mango (*Mangifera indica*), it is suspected that the poisonous principle may be present in very small quantities in the fruit. It is also well known that the lumber of *Gluta benghas*, exported at times from Malaya to Europe and the United States, may cause severe dermatitis among the millmen and carpenters who work with it.

The treatment is the same as for *Rhus* dermatitis. The irritating principle being a nonvolatile, irritating oil, any use of salves should be avoided, such treatments merely tend to spread the irritating principle. Thorough washing or scrubbing with a warm, strong, alkali soap solution is always indicated, bathing in alcohol is also of value. Merrill states that one of the most effective methods of treatment is to bathe the affected parts with ordinary photographic hypo (saturated solution of sodium hyposulfite).

TRENCH FOOT THE DIAGNOSTIC VALUE OF "ISCHEMIC PAIN" A E SCHECTER and CHARLES A RAGAN, Bull U S Army M Dept, June 1945, no 89, p 98

A type of pain brought on by vascular occlusion, which is seen almost exclusively in trench foot, is described. It is suggested that this pain is related to ischemia. It is believed that the severity of the local tissue damage in patients with trench foot can be correlated with the response to vascular occlusion. The procedure can be used to advantage in forward areas to determine accurately and promptly the diagnosis of trench foot. It is suggested that the term "ischemic pain" be applied to this phenomenon.

STRAKOSCH, Denver

A FIELD STUDY OF LATENT TULAREMIA IN RODENTS WITH A LIST OF ALL KNOWN NATURALLY INFECTED VERTEBRATES A L BURROUGHS, R HOLDENRIED, D S LONGANECKER and K F MEYER, J Infect Dis 76 115 (March-April) 1945

The authors found that latent tularemia infection was present in *Rattus norvegicus*, *Microtus californicus* and *Peromyscus maniculatus*. None of their ectoparasites were infected. The authors suggest the possibility of an air-borne transmission of tularemia among some rodents and include a list of vertebrates known to be naturally infected with tularemia.

CORNBLEET, Chicago

DERMATITIS EXFOLIATIVA FOLLOWING ARSPHENAMINE THERAPY OBSERVATIONS ON FIFTY CASES M J COSTELLO and S LANDY, New England J Med 232 369, 1945

Costello and Landy have observed 50 patients with exfoliative dermatitis attributable to arsphenamine, 26 women and 24 men, of whom 48 were improved or cured and 2 died. Forty-two had received neoarsphenamine, 2 had received oxophenarsine hydrochloride and 2 had received acetylglucoarsphenamine. Clinical jaundice occurred in 2 patients. Twenty-seven patients had a positive Wassermann reaction of the blood and 23 a negative one. Sodium thiosulfate administered to 30 patients proved of no value. Dextrose injected intravenously appeared to be of benefit. Crude liver extract administered intramuscularly had to be discontinued because of formation of abscesses. Recommendations for prevention and treatment are given.

AN EVALUATION OF SULFONAMIDE OINTMENT BASES R W HOWARD, New England J Med 232 698, 1945

According to the experimental studies of Howard if optimum therapeutic efficacy is to be realized all grease or cold cream bases for external applications of sulfonamide drugs should be avoided. Greasy bases obstruct the release of the drug. Moreover, they are not miscible with water, they are sticky and objectionable to the patients, and they are difficult to remove. High levels of sulfonamide compounds are released by oil in water emulsions, stearate vanishing creams, bentonite and pectin jelly bases.

A REVIEW OF RECENT FINDINGS IN FILARIASIS D R A WHARTON, New York State J Med 45 500, 1945

Because of the possibility of the introduction of filariasis into the United States with the return of the troops from the tropics, Wharton describes the various methods of diagnosing the disease—biopsy, finding of calcified worms by roentgenologic examination, presence of microfilarias in the blood and the cutaneous test. The treatment is symptomatic. Probably in many of the patients the infection will terminate spontaneously, and the menace to this country is relatively small.

MYCOSIS FUNGOIDES TWO UNUSUAL TYPES, ONE PRESENTING LEONINE FACIES, THE OTHER, PARAPSORIASIS (?) IN PATCHES FOR THIRTY YEARS E W ABRAMOWITZ and B KANEE, New York State J Med **45** 512, 1945

Two interesting cases of mycosis fungoides are described, one presenting a rare facial appearance resembling nodular leprosy and the other, presenting lesions of classic parapsoriasis for thirty years, later proved to be mycosis fungoides

A BRIEF HISTORY OF DERMATOLOGY IN NEW YORK CITY ITS SHARE IN THE PROGRESS OF THE SPECIALTY IN AMERICA P E BECHET, New York State J Med **45** 629, 1945

From the founding, in 1869, of the New York Dermatological Society, the oldest in the world, P E Bechet takes the reader through the beginning, in 1836, of American dermatology the opening by H D Bulkley of the Broome Street Infirmary for Diseases of the Skin, the appearance of the first journal on dermatology in 1870, the publication of Piffard's textbook on dermatology and the opening of the largest hospital for cutaneous diseases in America, the New York Skin and Cancer Hospital Highlights of the lives of Bulkley, Piffard, Fox, Sherwell, Keyes, Robinson, Morrow, Fordyce, Pullitzer and Taylor are given

RONCHESE, Providence, R I

NON-ACID-FAST FORMS OF THE MYCOBACTERIUM OF HUMAN LEPROSY ELEANOR ALEXANDER-JACKSON, Science **101** 563 (June 1) 1945

The author has developed a triple stain method which reveals non-acid-fast forms of Mycobacterium tuberculosis not disclosed by the usual Ziehl-Neelsen technic With this method, acid-fast tubercle bacilli stain red, non-acid-fast forms (rods, granules and zooglea) stain blue, while other organisms, tissue cells, etc, form a light green background

With this technic, nasal smears and smears from cutaneous lesions of patients with leprosy were studied Of the 34 patients, 84 per cent showed zooglic and granular or sporelike forms, 50 per cent showed zooglic forms only, 40 per cent showed some acid-fast forms and 34 per cent showed acid-fast or non-acid-fast rod forms

The author concludes that "while relatively few cases are reported here, and mycobacterium leprae cannot as yet be cultured on suitable media or successfully inoculated into animals in order to obtain absolute experimental proof, nevertheless, these findings strongly suggest that the mycobacterium of leprosy, like the mycobacterium of tuberculosis, has a zooglic form or phase The existence of non-acid-fast forms in leprosy may explain certain peculiarities in the course of the infection, such as its protracted incubation period, and the difficulty in demonstrating bacilli in certain types of lesions The results of this limited study would seem to encourage more extensive observations with the aid of the Triple Stain Technic"

RATTNER, Chicago

ERYTHEMA MULTIFORME WERNER W DUEMLING and THEODORE A LESNEY, U S Nav M Bull **44** 968 (May) 1945

Ten cases of primary erythema multiforme are reported, all observed during the spring In every case there was involvement of the oral mucosa, and differentiation from aphthous stomatitis, Vincent's angina, pemphigus and syphilis was required

The average age of the patients was 22 years The average temperature was 100 F, and the average duration of symptoms was 111 days There was no particular racial distribution, all Kahn tests of the blood elicited negative reactions, and the cultures showed the usual saprophytic organisms

**FILARIASIS HISTOPATHOLOGIC STUDY** PAUL MICHAEL, U S Nav M Bull  
45 225 (Aug ) 1945

On the basis of laboratory studies, the author concludes that filariasis should not constitute a public health problem in the continental United States and that instances of physical damage to the patient should be negligible. The immune reactions of the host together with the reticuloendothelial system are sufficient to destroy the parasite in most instances, provided the patients are evacuated from the endemic areas.

The presence of the parasite in the host initiates a characteristic foreign body granulomatous reaction. Many of the cutaneous manifestations seen in filariasis are presumed to be allergic in nature. For diagnostic purposes the laboratory method of choice is histologic examination of suspected lesions, for the examination of the blood for microfilarias is often inadequate.

The article includes eight excellent histopathologic illustrations in color.

ROBIN, South Bend, Ind

**SCABIES PROPHYLAXIS WITH "TETMOSOL" SOAP** KENNETH MELLANBY, Brit M J 1 38 (Jan 13) 1945

Using a soap which contains 10 per cent Tetmosol (tetraethylthiuram monosulfide) Mellanby was able to control an epidemic of scabies in a mental disease hospital.

Eleven weeks after the onset of a heavy infestation most patients were cured and the spread of the disease was prevented.

**PENICILLIN IN GONORRHOEA AND SYPHILIS** F L LYDON and W R SCOTT COWE, Brit M J 1 110 (Jan 27) 1945

The present dose of penicillin used in the treatment of gonorrhoea is approximately 100,000 units, a dose quite inadequate to cure syphilis but perfectly adequate to heal a primary lesion and influence, at least temporarily, the serologic reaction for syphilis.

The authors raise three theoretic questions without attempting answers at this time. 1. What interval must elapse before a positive Wassermann reaction or systemic manifestations of syphilis will develop in such an inadequately treated patient? 2. On the analogy that early syphilis inadequately treated with the arsenicals frequently exhibits precocious tertiary lesions, will this also hold true for early syphilis inadequately treated with penicillin? 3. On the same analogy, is not such a patient likely to remain infective during the assumed latent period?

**IMPETIGO TREATED WITH SODIUM PENICILLIN CREAM** J MUNRO GOLD, Brit M J 1 152 (Feb 3) 1945

The author succeeded in curing a patient with severe impetigo with a cream consisting of equal parts of hydrous wool fat, cod liver oil and water, to which was added enough sodium penicillin to make a cream of 500 Oxford units per gram.

SHAW, Chattanooga, Tenn

**INCIDENCE OF SCABIES IN A COMMUNITY USING ORDINARY SOAP AND TETMOSOL SOAP** W BARTLEY, K UNSWORTH and R M GORDON, Brit M J 1 332 (March 19) 1945

The incidence of scabies in a closed community of 400 persons was observed over a period of thirty-one weeks, during the last thirteen of which Tetmosol soap was substituted for ordinary toilet soap.

During the eighteen weeks in which ordinary soap was used the incidence of scabies increased from 4 per cent to 92 per cent and 21 new cases were recorded. At the end of this period soap containing 5 per cent tetmosol (tetraethylthiuram monosulfide) was substituted for ordinary soap. During the remaining thirteen weeks of observation the incidence of scabies fell from 92 to 0.5 per cent and only 1 new case occurred. No cases of dermatitis were recorded.

SUBSTANCES USED FOR PEDICULOSIS CAPITIS ELIZABETH SCORBIE, Brit M J. 1 409 (March 24) 1945

DDT emulsion and lethane hair oil are the two insecticides of outstanding value in the treatment of pediculosis. DDT is preferable because one treatment properly carried out should produce cure in every case, and the odor is not unpleasant.

Since DDT is insoluble in water, the hair can be washed without affecting its action. No toxic effect or irritation of the skin has been noted after the use of lethane hair oil or DDT emulsion.

A CASE OF DDT POISONING IN MAN V B WIGGLESWORTH, Brit M J 1 517 (April 14) 1945

The subject was a healthy laboratory worker who was attempting to determine whether DDT (dichlorodiphenyltrichloroethane) was liable to cause any local irritation. He deliberately allowed small quantities of acetone solution of DDT to evaporate on the back of his hand and further permitted the hands to be immersed in a solution of DDT for several minutes. Within the day symptoms developed, consisting of a feeling of heaviness and aching in the extremities and weakness in the legs. Symptoms became progressively worse until sleep became almost impossible because of periods of extreme nervous tension and involuntary muscular tremors. The subject had not recovered at the end of ten weeks. The case recorded is one of deliberate exposure to amounts of DDT far in excess of any that would be likely to be encountered in practice.

HYPERTRICHOSIS WITH MENTAL CHANGES EFFECT OF ADRENALECTOMY  
RAYMOND GREENL, A SPENCER PATERSON and G C L PILR, Brit M J 1 698 (May 19) 1945

A case of hypertrichosis associated with mental changes which gradually resolved after adrenalectomy is reported. Within two months after operation there was no sign of further growth of hair.

TREATMENT OF IMPETIGO MARY S SMITH and E COLIN JONES, Brit M J 1 699 (May 19) 1945

The authors feel that antiseptics are not necessary in the successful treatment of impetigo. They recommend a method of treatment with simple calamine liniment which depends on the following six principles: first, exposure of all parts to treatment—by shaving if necessary; second, avoidance of trauma; third, insuring that the dressings are kept in close contact with the affected parts and that they remain moist; fourth, removal of dressings for only the few minutes necessary for shaving or redressing and immediate reapplication; fifth, inclusion of all outlying lesions in the treatment with the dressing extending about 1 inch (2.5 cm) beyond the borders; and sixth, alteration in the method of applying the medicament as occasion demands—e.g., from compresses to smears—with no alteration in the remedy itself.

SHAW, Chattanooga, Tenn

# Society Transactions

## NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

Harry C. Saunders, M.D., *Chairman*

Frank Vero, M.D., *Secretary*

Dec 5, 1944

### **Pemphigus Vegetans** Presented by DR TIMOTHY J. RIORDAN

T. C., a woman aged 52, was admitted to Bellevue Hospital on July 18, 1944. About eight months prior to admission "blisters" developed on the lips, roof of the mouth, tongue and buccal mucosa. For six months the lesions were confined to these areas. About two months before admission new lesions developed on the scalp and in the axillas, groin and intermammary folds. Examination of the skin showed bullae varying from a few millimeters to 1.5 cm in diameter on the forehead, commissures of the mouth, upper lip, chin, axillas and groin. In the mouth there were bullae and ulcerations involving the palate, tongue and buccal mucosa.

About six to seven weeks after the patient was admitted to the hospital several discrete, moist vegetative lesions developed in the axillas, in the groin and in the left intermammary area. These lesions gradually developed a flat, smooth surface, erythematous in appearance. Under continued treatment, the lesions regressed, leaving pigmented areas.

Laboratory studies showed the urine to be normal, and the Wassermann reaction of the blood negative, a blood count showed 12,250 leukocytes, with 71 per cent polymorphonuclear leukocytes, 15 per cent lymphocytes, 8 per cent monocytes and 6 per cent eosinophils.

The patient was given carbarsone tablets. Beginning with 0.25 Gm a day, the dose was increased to 0.75 Gm daily. The total amount given was 16 Gm.

### DISCUSSION

DR E. WILLIAM ABRAMOWITZ: The bullous and vegetating lesions lasted about eight or ten months, rather an accelerated pace for a benign pemphigus. The patient is apparently in good health now and was not extremely sick during the entire time. Judging from the pigmentation and the configuration now present, I think that there is a possibility that the eruption is of the erythema multiforme fixed type, possibly resulting from a drug. The patient is entirely too insistent on the fact that she takes no drugs. There are few persons who do not take some medicines at one time or another.

DR FRANK C. COMBES: This case is an interesting one from several standpoints. Ordinary pemphigus vulgaris—and by that the bullous type is usually meant—is characterized by alternating periods of exacerbation and remission. Many patients will get over their first siege without a great deal of difficulty, no matter what medicine is used. The second exacerbation will be stormier, and during the third it does not matter greatly what therapy is used. Pemphigus foliaceus and pemphigus vegetans are both usually gradually progressive, without remission. This case I have watched for some time. The patient had all the earmarks of pemphigus, if there are such things, with bullae particularly in the mouth and around the lips and hypoproteinemia with inversion of the albumin-globulin ratio, on which much importance is placed. This patient had tremendous vegetative lesions in the axillas, and there is no doubt in my mind that the diagnosis is pemphigus.



DR LOUIS TULIPAN I also observed this case for a long time, and I feel that the diagnosis was correct. Am I to understand that Dr Abramowitz means that if a case runs on for ten months with benign symptoms the diagnosis should be changed?

DR TIMOTHY J RIORDAN I am grateful for the discussion of this case. I should like to mention that one of my reasons for presenting the case is to show the favorable response to a pentavalent arsenical, carbarsone (4-carbamidophenyl-arsonic acid) given at Bellevue Hospital at the suggestion of Dr Robert P Little, who is now preparing a preliminary report on these cases.

#### **Pernio with Milia** Presented by DR TIMOTHY J RIORDAN

M L, a man aged 47, is presented from St Vincent's Hospital, with an eruption of the ear lobes of ten months' duration. The patient has worked in a butcher plant for twenty years, spending eight to ten hours daily in the refrigerator at a temperature of 14 to 34 F. Ten months ago he noticed itching, burning and swelling of the lobes of the ears.

Examination shows a heavy-set man with flushed face and cyanotic skin and ears. The ear lobes are tumefied and red and are studded with numerous pinhead-sized yellow milia which on acupuncture yield sebaceous, cheesy material. There are numerous lanugo hairs.

Laboratory examination showed that the urine was normal. The blood count showed hemoglobin, 100 per cent, red blood cells, 5,100,000, and white blood cells, 5,000, with 60 per cent polymorphonuclear leukocytes, 36 per cent lymphocytes and 4 per cent monocytes. The tuberculin test elicited a strongly positive reaction in a dilution of 1:100,000. Guinea pig inoculation gave negative results, even after prolonged observation. Roentgenologic examination of the chest showed the heart to measure 17 cm in its transverse axis, which is slightly over average normal measurement. The aorta was moderately dilated. There was congestion in the central zones and bases of the lungs but no evidence of recent parenchymal infiltration or pleural involvement. There is billowing of both sides of the diaphragm.

Biopsy showed the epidermis to be extremely thin. In the corium were found small epidermoid cysts filled with keratin. Between the cysts, the corium was densely infiltrated with lymphocytes and larger reticuloendothelial cells.

#### **DISCUSSION**

DR MAX SCHEER The diagnosis of pernio, I think, is correct. The presence of milia is an unusual feature. I do not recall having seen it before in pernio.

DR JACK WOLF I think that Dr Scheer's remarks are well taken. This is a favored site for small sebaceous cysts, and I think that is a more likely diagnosis than milia. I also noticed comedo-like lesions.

DR TIMOTHY J RIORDAN In connection with Dr Wolf's remarks about sebaceous cysts, these lesions were true milia and not at all like the steatomas I noted at first. I found that it was difficult to remove the milia. They were keratin balls and not sebaceous material, as mentioned in the report. Incidentally, in that particular area I found a practical method of removing the milia. I used a mouse tooth forceps, clamped the milium and broke the skin at the base, and it shelled out readily.

I thought that some of these lesions bore a resemblance to tuberculosis, and the case was carefully studied, with roentgenologic examination of the chest and inoculations of a guinea pig. After two or three months the results of the latter were negative and the Mantoux test was strongly positive. The response to the removal of milia was striking. Of course, the man was warned about exposure to cold by going into the refrigerator in the course of his work.

**Lichen Sclerosus et Atrophicus (Hallopeau)** Presented by DR TIMOTHY J RIORDAN

C N, a white woman is presented from St Vincent's Hospital, with an eruption on the neck and chest of fifteen months' duration. There are four alabaster white, hidebound patches up to 2 inches by  $\frac{3}{4}$  inch (5 by 19 cm) in diameter above and below the clavicle and the sides of the neck and chest, with a 2 mm pink areola, and several pinhead-sized white satellite atrophic lesions.

The Wassermann reaction of the blood was negative, the urine was normal and the blood count showed 90 per cent hemoglobin, 4,950,000 red blood cells and 9,500 white blood cells, with 76 per cent polymorphonuclear leukocytes and 24 per cent lymphocytes.

Biopsy showed the epidermis to be atrophic. In one area there was a piling-up of atrophic-looking prickly cells. In the corium there was a mild round cell infiltration. The granular layer was beaded, and in the subepidermal spaces there were casual areas of cellular elements pushed close to the epidermis, suggesting lichen planus.

## DISCUSSION

DR FRANK C COMBES: This case had all the clinical characteristics of the disease as presented. I think that the eruption is a perfect example of this dermatosis and agree with the original diagnosis.

DR MAX SCHFFER: This patient also presented in some lesions the horny plugs which are found in this disease at least in the early stage. Later I understand, these plugs fall out and disappear.

**A Case for Diagnosis (Boeck's Sarcoid?)** Presented by DR TIMOTHY J RIORDAN

M S, a white woman aged 55 is presented from St Vincent's Hospital, with a lesion on the left side of the nose, of eight months' duration.

Examination discloses a small cherry-sized, nonpainful, erythematous infiltrated patch on the left side of the nose in the region of the lacrimal sac. There is no history of injury or disease of the eye.

The Wassermann reaction of the blood was negative, and the urine was essentially normal. Roentgenologic examination after injection of iodized poppyseed oil into the left lacrimal sac revealed normal conditions. Roentgenologic examination of the paranasal sinuses showed the frontal sinuses to be of average size, without pathologic changes. The ethmoid sinuses showed chronic involvement on both sides. The antrums were asymmetric, the right being smaller. Some mucosal thickening was seen in the floor and lateral wall of the right antrum. The sphenoid sinuses showed nothing unusual.

Biopsy showed a tiny bit of white tissue which consisted of corium containing many sebaceous and sweat glands.

## DISCUSSION

DR EUGENE TRAUOGOTT BERNSTEIN: I agree with Dr Rosen that one is dealing here with Boeck's sarcoid. It is a question whether the related conditions of Boeck's sarcoid, Darier's sarcoid, lupus pernio, erythema induratum, tuberculosis nodularis of the hypodermis, benign lymphogranulomatosis, osteitis tuberculosa multiplex cystoides and similar disorders should not be plainly named sarcoidosis. I should like to ask whether these diseases should continue to have different names, or should all these entities be placed under the term sarcoidosis?

DR MAURICE J COSTELLO: I agree with the diagnosis.

DR CHARLES WOLF: I believe that this solitary lesion has some features which one may consider as possibly of a malignant nature. The patient has seborrheic dermatitis, which is incidental. The inner canthus of the eye is a favorite site for epithelioma, and the patient is at the age when epithelioma is more apt to develop. Sarcoid or sarcoidosis is a disease of early or middle life. I therefore suggest another biopsy.

DR FRANK C COMBES I do not think that the diagnosis of sarcoid should be accepted too quickly in this case. It is a possibility, but I do not think that there is enough evidence at present to justify it. There are no clinical systemic characteristics of sarcoid. On further investigation this may prove to be a case of that disease, but it appeared to me that one may be dealing with a type of scrofuloderma or some other type of tuberculosis. There is, however, no history of tuberculosis in the family. I believe that the patient should have a complete study, including tuberculin tests. Anergy would point toward sarcoid and hyperergy to scrofuloderma.

DR MAURICE J COSTELLO I agree with the diagnosis as presented, but I thought on palpating the lesion that it was a little softer than one would expect to find in sarcoid. This is the most common location for a single lesion of sarcoid. I think that a favorable response to roentgen rays would be in favor of sarcoid and against lupus erythematosus. Tuberculin studies should be carried out.

DR ISADORE ROSEN This condition should be recognized by the microscopic examination. It is difficult for one to make a diagnosis from the clinical features alone, because sarcoids may vary in appearance from that of granuloma annulare to that of lupus tumidus. Age does not play an important role in differential diagnosis.

DR TIMOTHY J RIORDAN As to the remarks of one speaker about lupus erythematosus, at no time during the course of this lesion was there any evidence of scaling. It remained the same, with a shiny surface. I agree that a biopsy is important in establishing a diagnosis in this case. I think that Dr. Combes' suggestion of the possibility of the scrofuloderma type of tuberculosis is good. In the case of a shiny lesion without any definite nodular border or waxy appearance, I thought that I could rule out epithelioma, though not entirely. As a matter of fact, when I first saw the patient, the differential diagnosis was between sarcoid and epithelioma.

#### Secondary Syphilis Condyloma Latum in the Nostrils Presented by DR GIRSCH D ASTRACHAN

A. D. S., a man aged 46, born in Italy, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Nov. 9, 1944, with the history of an eruption in the nostrils of a few weeks' duration. The patient noticed some difficulty in breathing through his nose, he found a small pimple in the right nostril which had greatly increased in size by the following week. At that time the same kind of lesion appeared in the left nostril. The patient also recollected having had a slight swelling of the penis about four months ago.

Examination disclosed in both nostrils, attached to the lateral aspects, dime-sized to nickel-sized, elevated, dark gray, button-like, somewhat indurated, partly verrucous and partly smooth lesions. These obliterated the larger part of the orifice of the nostrils. The patient also presented around the anal region three pea-sized to bean-sized, well defined, elevated, indurated, round, flat, papular lesions, covered with a gray membrane. A dark field examination of the serum from one of the perianal lesions showed the presence of *Treponema pallidum*.

The patient was treated with penicillin and dichlorophenarsine hydrochloride from November 22 to November 24, receiving a total of 1,800,000 units of penicillin and 375 mg. of dichlorophenarsine hydrochloride. The lesions in the nostrils and around the anus showed a definite improvement.

Examination on Dec. 2, 1944 showed on the lateral aspect of both nostrils several flat, dark gray, pea-sized, elevated, soft, closely set lesions with rough surfaces. Around the anus are seen three small, pea-sized, elevated, gray papular lesions.

The serologic reaction of the blood was positive on two occasions (November 16 and 28). The complete blood count was normal except for a slight anemia (red blood cells 4,200,000) and leukocytosis (white blood cells 12,100). On November 24, after two days of therapy with penicillin, the blood count was normal. The leuko-

cyte count decreased to 10,500. The urine was normal. The icterus index was 9.4 on November 25.

Histologic examination by Dr. Charles Sims confirmed the diagnosis of secondary syphilis.

#### DISCUSSION

DR GIRSCH D. ASTRACHAN: I presented this case because of the unusual location of the condylomas. I have never seen a case of this kind, nor have some of my associates with whom I discussed the problem. Another interesting feature in this case is the change in the blood count following two days of penicillin therapy. The number of red blood cells increased from 4,200,000 to 5,250,000, and the white blood cells decreased from 12,100 to 10,550.

#### Atopic Eczema (Allergic Eczema) Presented by DR H. VICTOR MENDELSON

M. W., a woman aged 32, was admitted to Bellevue Hospital on Oct. 10, 1944. The history disclosed that the patient had eczema in childhood, up to the age of 7 years. From the age of 7 to 13 she was free of cutaneous eruption. At the age of 13 she had a recurrence of the eczema, with remissions and exacerbations up to the age of 26, when her second child was born. From that time on, the patient has not been entirely free from cutaneous lesions. In addition, recurrent attacks of asthma began to develop, the last attack occurring about three months ago. The present dermatologic exacerbation began during the summer, with dryness, roughening and a tendency toward cracking of the skin of the legs, thighs and abdomen. Later her face, neck, arms and hands became involved, and finally the skin of the entire body was affected. At times the skin would be so dry that there was considerable scale formation. Two years ago the patient underwent scratch tests at the Long Island College Clinic and reacted positively to many foods. Avoidance of these foods has had no effect on the eruption.

Examination of the skin showed a generalized dermatitis, which was especially pronounced on the face, neck, chest, extremities and genital area, characterized by an erythematous, lichenified, dry, leathery surface, with many adherent, moderately thick scales and crusts. There were moist areas on the upper lips as well as on both postauricular regions and the posterior surface of the neck. On the back and abdomen there were many papules, yellowish white in appearance and 3 to 6 mm in diameter, some with hemorrhagic centers. The left genitocrural area showed erythema.

The urine was normal. The white blood cell count showed 19,000 leukocytes, with polymorphonuclears 45 per cent, lymphocytes 27 per cent, eosinophils 21 per cent, monocytes 4 per cent, transitional cells 2 per cent and basophils 1 per cent. The Wassermann reaction of the blood was negative.

Treatment consisted of (1) fever therapy, by the administration of gradually increasing doses of typhoid vaccine intravenously, (2) ultraviolet irradiation therapy, (3) aolan (sterile solution of lactalbumin in colloidal form) intramuscularly, and (4) topical applications.

The patient has shown definite improvement during hospitalization. The extreme dryness and roughness of the skin have diminished, the moist areas have disappeared, and the pruritus is much less.

#### DISCUSSION

DR E. WILLIAM ABRAMOWITZ: The treatment of such patients is unsatisfactory from every standpoint. The determination of the allergic status is usually not of much help. Every one has seen patients who have had this disease from childhood. Sometimes it disappears after several years, and sometimes it lasts until the age of 30 or 40. The improvement in this case with fever therapy is only temporary. I think that the emotional element is of importance, because emotional upsets will bring about a recurrence. This is the type of disease which comes under the classification of psychosomatic disorders. When patients are removed from their usual

environment, they improve greatly. The crusted excoriations on the skin of the arms are like neurotic excoriations, but the lichenification present indicates what is called atopic dermatitis.

DR ABRAHAM WALZER. I should like to discuss two aspects of this question. First, the name. The original conception of this disease was given by the French school (Vidal, Brocq and Besnier—especially the last), and they described the entity as neurodermatitis. If one takes their description and conception of this disease and compares them with the present conception of atopic eczema, it will be noted that the two are practically the same. If the term "allergy" is substituted for their "diathesis," one gets the present conception of neurodermatitis.

Second, the allergic aspect. By labeling this condition atopic eczema, I think that Dr. Mendelsohn should have made an attempt to connect it with allergy. There is a definite family history of asthma, and the patient also suffers from it. This woman therefore, has atopy. Direct testing of these patients is of no value. The skin of persons with neurodermatitis will often give false reactions. Indirect testing must be employed.

In treatment, elimination of offending allergens is not the only thing to be done. These patients have scratched for years and have produced a dermatitis which is more or less fixed. With local treatment and elimination of allergens, 75 per cent benefit can be obtained. These patients, however, will often improve temporarily with almost any treatment or with none. In other words, remissions and relapses are common in the course of the disease. The improvement following the injection of typhoid vaccine or psychotherapy, therefore, just represents the natural course of the disease and not the value of this specific therapy.

DR EUGENE TRAUGOTT BERNSTEIN. I do not intend to harp on the subject of psychosomatic cutaneous disorders. The skin is the mirror of the soul, one really does not know how imponderable psychic influences may affect the physical being to the extent that the person may drop dead. The skin as an expressive organ reflects emotional states from within and responds to psychic insults from without. The psychologic aspect plays an important part in the treatment of disorders of the skin. It is known that when a patient is given a new therapy, be it an injection of vitamin B, a salve, the reassurance of a new physician or other psychologic influences, the skin may improve dramatically in a short time, then, as the patient stays with the physician for a time, there is an exacerbation of the original condition. There is no doubt that a strong connection exists between psychic influences, emotional upsets, unpleasant environment and the states of acuity or amelioration of the cutaneous disorder. In cases of dermatologic disorders with a psychologic aspect, the patient should be subjected to neuropsychiatric treatment. I think that the present restless time is responsible for the "no man's land" where dermatology and psychiatry meet. Each of these specialties has its boundaries, beyond which it is unwise to transgress, but the cooperation between dermatologists and psychiatrists should prove mutually constructive and profitable.

DR H. VICTOR MENDELSON. This case was presented not for the purpose of demonstrating a new or specific type of treatment in cases of atopic eczema generally but rather to show that in this instance improvement was largely due to this form of therapy and was not the result of change of environment alone. I was glad to hear Dr. Abramowitz call attention to the emotional factors in the causation of these eruptions. In my opinion, the importance of this fact cannot be overemphasized. Treatment in most if not in all cases of atopic eczema should include the correction of neurogenic and emotional disturbances.

Dr. Walzer raised a number of interesting questions which I should like to discuss at great length, but the lateness of the hour permits only brief references. I thoroughly agree with him that this patient should not be tested by the scratch or intradermal method, with her skin in the present condition. Such patients, however, can receive these tests during periods of remission, when they present ample areas of normal skin. The indirect method of testing has many advantages over the direct methods. The former, besides permitting the testing of patients

who present no healthy skin, also enables the demonstration of specific antibodies for certain allergens in the patients' serum. Nevertheless, even with this method of testing, the actual demonstration of causative agents in atopic eczema and other dermatoses has not been successful in my hands.

In 1934 I reported an allergic study of 262 cases of various dermatoses, including 86 cases of eczema, most of which were atopic eczema (*Sensitization Tests: Their Value in Dermatology*, *ARCH DERMAT & SYPH* 29 845 [June] 1934). Direct, indirect and patch tests were performed. This study was carefully carried out, some of the patients were observed over a period of three to four years. Collectively, the patients with atopic eczema gave a large number of positive reactions, but the ingestion or avoidance of the positively reacting substances had little or no effect on the disease. The cause was demonstrated in 1 case and partially demonstrated in 8 others. Atopic eczema is indeed a complex problem, the causation and the therapy of which are still uncertain.

I agree with Dr. Walzer that the terms flexural eczema, neurodermatitis, neurodermite, neurodermatitis disseminata, atopic eczema and atopic dermatitis are not clear in the minds of many dermatologists. May I add to this list the terms eczema and dermatitis? In reading reports dealing with eczematous eruptions, one frequently does not know what the writer had in mind. The disease entity which this patient presents is designated by the official nomenclature as atopic eczema (neurodermatitis disseminata).

#### HAWAII DERMATOLOGICAL SOCIETY

James T. Wayson, M.D., *President*

Harry L. Arnold Jr., M.D., *Secretary*

Dec 9, 1944

#### A Case for Diagnosis (Pityriasis-Rosea-like, Lichen-Planus-like Eruption Following Antisymphilitic Therapy?) Presented by DR. HAROLD M. JOHNSON

A 34 year old Filipino had been treated for syphilis since May 31, 1944. He received a course of bismuth and a course of arsenic (oxophenarsine hydrochloride), and when bismuth was started again, on Sept 20, 1944, a pruritic scaly exanthem with discrete scaly macules and papules following the lines of cleavage developed on his chest, arms and legs. The lesions are definitely pityriasis-rosea-like, with the dusky purplish hue of lichen planus. The patient complained of severe itching in periodic seizures. Antisymphilitic therapy was discontinued, and a plantation physician gave the patient sodium thiosulfate and calcium gluconate intravenously and antipruritic lotions.

He was seen on Dec 4, 1944, and a specimen for biopsy was taken from a typical scaly purplish papule located on his abdomen. The blood and urine were normal.

Biopsy showed hyperkeratosis of the horny layer, prickle cell metaplasia of the basal layer, with sharp-pointed rete pegs, a dense lymphocytic infiltrate in the corium, tightly packed against the epidermis, and abundant chromatophores. It was regarded as characteristic of lichen planus.

#### DISCUSSION

DR. HARRY L. ARNOLD JR. I thought that this patient had annular atrophic lichen planus.

CAPT. HERBERT LAWRENCE, M.C., A.U.S. In Los Angeles, about five years ago, there was much interest in eruptions following the administration of bismuth, which had not been observed previously. Clinically, this case is identical with some of the cases that were seen there at that time.

DR HARRY L ARNOLD JR By "identical" do you mean that the lesions were elevated, infiltrated annules with depressed hyperpigmented centers like those of this man? The eruptions of this sort that I recall seeing at meetings of the Detroit Dermatological Society at about that time were almost all pityriasis-rosea-like eruptions, chiefly in Negroes, in which hypopigmentation was the principal feature of the lesions

CAPT HERBERT LAWRENCE, M C, A U S There are two distinct morphologic pictures a pityriasis-rosea-like eruption without hyperpigmentation and a lichen-planus-like eruption with hyperpigmentation Rarely both eruptions would appear in 1 patient

DR HAROLD M JOHNSON I have seen pityriasis rosea following the administration of both bismuth and arsenic, but this is the first time I have seen lichen planus following the administration of bismuth

CAPT HERBERT LAWRENCE, M C, A U S At the time of which I speak, it was noted that since lichen planus usually responded well to injections of bismuth it was odd that the eruption should follow the administration of bismuth However, I have seen a patient with lichen planus who became much worse and in whom bullous lesions developed after the administration of bismuth

DR HAROLD M JOHNSON I have started this man on intramuscular injections of bichloride of mercury three times a week, and I also gave him an injection of mercuric salicylarsonate this morning

CAPT HERBERT LAWRENCE, M C, A U S It is of particular interest that this eruption followed not the initial administration but the readministration of bismuth after a period during which no bismuth was given This suggests a latent period, during which sensitivity developed

CAPT IRVING N HOITZMAN, M C, A U S (by invitation) I think that it is lichen planus It may be due to bismuth

CAPT L H ROSENTHAL, M C, A U S I agree with the diagnosis Lichen planus may have multiple causes, and it may be produced by injections of almost any of the heavy metals

#### **Lichen Nitidus** Presented by DR HAROLD M JOHNSON

A 7 year old Chinese schoolboy gave a history of a generalized eruption which had begun in January 1944 The lesions began on his abdomen and gradually spread to cover his entire body except palms, soles, scalp and lips The patient was not ill and had no subjective symptoms In June 1944 the rash disappeared after an attack of measles, but it returned one month later The father had a history of tuberculosis, the child's past history was otherwise essentially non-contributory

The patient presents a profuse generalized eruption of flat-topped, pinhead-sized, flesh-colored papules, which do not coalesce The lesions are so close that they present a nutmeg grater appearance in some areas There are several areas where Koebner's phenomenon is well shown, the papules being arranged in fine linear streaks The genitalia are covered with the minute millet seed papules The hard palate has a small papular patch

The blood was normal with the exception of eosinophilia of 3 per cent A roentgenogram of the chest was noncontributory The Mantoux test elicited a negative reaction

Treatment has consisted of the administration of vitamin A, 150,000 units daily, and weekly injections of bismuth subsalicylate (40 mg)

The biopsy showed a sharply outlined infiltrate of epithelioid cells and lymphocytes situated in the papillary layer of the corium, with the epidermis displaced abruptly upward over it

**Lichen Scrofulosus (Tuberculosis Lichenoides)** Presented by DR HARRY L ARNOLD JR

A 12 year old part-Hawaiian boy was presented a year ago with a diagnosis of lichen scrofulosus, which was not confirmed by biopsy, and with only a weakly positive reaction of the skin to 0.005 mg of purified protein derivative of tuberculin.

Under treatment with cod liver oil orally, the eruption slowly increased in extent and severity until February 1944, when, after a mild sunburn, the whole eruption subsided completely. In November the patient experienced a relapse, and he now presents about the same appearance as before. The clinical resemblance to lichen nitidus is somewhat more striking now than at the time of his last presentation.

## DISCUSSION OF THE TWO PRECEDING CASES

DR HAROLD M JOHNSON I should like to point out that the typical histologic changes of lichen nitidus were found only after repeated sections had been cut from the biopsy specimen. Ellis and Hill have suggested that lichen nitidus is a variant of lichen planus, and on that basis I have treated this boy with bismuth. It is interesting that the eruption cleared completely after an attack of measles in June but that the patient had a recurrence.

CAPT DAVID MUSMAN, M C, A U S Why do you not give him human measles immune globulin?

DR HARRY L ARNOLD JR In regard to the boy presented as having lichen scrofulosus, I must admit that neither the histologic changes nor the weakly positive reaction to purified protein derivative of tuberculin is particularly consistent with the diagnosis. I recently noted that the illustrations of the histologic changes of lichen scrofulosus in Sutton's text are as good pictures of lichen nitidus as those given under the heading of lichen nitidus, or perhaps even better.

CAPT L H ROSENTHAL, M C, A U S Pinkus, in his original description of lichen nitidus, classified it as a tuberculid.

DR HARRY L ARNOLD JR Does any one have any suggestions for the treatment of the boy with the lichen scrofulosus?

DR HAROLD M JOHNSON Is it lichen scrofulosus?

CAPT IRVING N HOLTZMAN, M C, A U S (by invitation) Clinically, it certainly looks like it.

DR HAROLD M JOHNSON I should suggest the administration of vitamin A, 300,000 to 500,000 units daily. It looks to me as if it might be phrynoderma.

**Subacute Disseminated Lupus Erythematosus** Presented by DR HARRY L ARNOLD JR

A 23 year old white housewife, previously presented before this group with a disease shown as an example of subacute disseminated lupus erythematosus, is presented again to show (1) the failure of 200,000 units of penicillin given intramuscularly in forty-eight hours to affect her condition, (2) the persistence of hypocholesterolemia, at a level of 57 mg per hundred cubic centimeters in September and 69 mg now, despite a basal metabolic rate only 14 per cent above normal, and (3) the effect of strong solution of iodine U S P, 5 drops twice daily. Since she has taken strong solution of iodine (seven weeks) she has felt better and has gained weight, the white blood cell count has dropped from 6,000 to 4,000 and from 77 to 67 per cent polymorphonuclear leukocytes, the erythema multiforme has become somewhat severer and more extensive, there was a period of nearly three weeks during which she was uncomfortable as the result of a diaphragmatic pleurisy on the left, the sedimentation rate has remained close to 60 per cent, and the Weltmann coagulation band has remained at 8. The urine still shows no abnormality.

The patient is also presented for suggestions as to treatment and for opinions as to the advisability of trying penicillin again in a more nearly adequate dosage.



## DISCUSSION

DR HARRY L. ARNOLD JR. Dr Herman Beerman recently told me that a patient with this disease treated with penicillin some months ago in Philadelphia is still getting along well. However, it is listed as one of the diseases in which the administration of penicillin is useless. I think that every one would agree that the trial of penicillin previously made in this case was inadequate because of the small dose. I think that a larger amount of the drug can be obtained for her now.

It was the consensus of the members that penicillin was worth trying again in more nearly adequate dosage.

NOTE.—Penicillin, in a total dose of 2,000,000 units in eight days, had no beneficial effect whatever.

**Epidermolysis Bullosa** Presented by DR HAROLD M. JOHNSON

A 7 month old Japanese girl was first seen on Sept. 22, 1944. There was a history of chronic, crusted, impetiginous lesions on the dorsa of the feet, hands, knees and elbows since birth. Dime-sized to quarter-sized bullous lesions would appear on the plantar surface of the feet and heels after moderate trauma.

An uncle had the same type of dermatosis at birth, but it gradually disappeared.

Physical examination shows a well developed baby with many old healed scars on the plantar surface of the feet and heels. There are several bullous lesions on the dorsa of her hands. There is a suggestion of early epidermal denudement on the vulva. The mucous membranes of the mouth and the nails are not involved.

## DISCUSSION

The members agreed with the diagnosis as presented.

**Dermatitis Herpetiformis** Presented by DR HAROLD M. JOHNSON

A 13 year old Chinese boy was first seen on Nov. 15, 1944, with a history of an extremely pruritic dermatitis of his legs, buttocks, shoulders and arms, which had been present for five years. The family history and the past history are irrelevant.

Examination reveals an excoriated vesicular-papular rash in symmetric grouped arrangement. There is pigmentation and scarring of old, healed lesions. Mild secondary infection was noted in some patches after they had been scratched.

The course of the disease had been variable. There were many periods of quiescence followed by episodes of extreme pruritus. The patient has seen several physicians, with considerable relief in some instances. He previously received sulfathiazole and sulfapyridine by mouth, with moderate but incomplete relief.

A hemogram on Dec. 8, 1944 showed a hemoglobin content of 71 per cent, red cells 4,390,000, white cells 8,400, polymorphonuclear leukocytes 48 per cent, lymphocytes 45 per cent, eosinophils 4 per cent and monocytes 3 per cent. There had previously been a 28 per cent eosinophilia in the vesicle fluid.

An intramuscular injection of bismarsen, 0.1 Gm., was followed by relief of itching within a few days. The administration of the drug is being continued.

## DISCUSSION

DR HARRY L. ARNOLD JR. The response to bismarsen is interesting if it is not just another spontaneous remission.

**Dermatitis Herpetiformis** Presented by DR HAROLD M. JOHNSON

A 27 year old white woman came to the office on Dec. 8, 1944, with a history of a severely pruritic dermatitis of the back, chest and thighs since the age of 13. The lesions have been papular, with occasional vesicles which appear in crops. The lesions and pruritus disappeared several years ago, after a mild illness producing a temperature of 103 F., but promptly returned in a few days, after the convalescence. The patient has been seen by many dermatologists on the mainland and has received as many diagnoses.

The patient is a highstrung, underweight woman whose entire back is covered with excoriated papules. There are extensive hyperpigmentation and scarring, showing evidence of old lesions. The same process can be seen on the chest. The thighs and arms have only scattered excoriated papules.

Treatment has included administration of sulfonamide drugs and arsenic intravenously, intramuscularly and orally. Many antipruritics have been used, without much help. The patient has no record of preparations or exact dosage used.

The blood count showed a slight leukopenia (4,000 white blood cells per cubic millimeter). There were no eosinophils. There has not been time for a biopsy or other laboratory studies.

#### DISCUSSION

DR HARRY L. ARNOLD JR. I agree that the duration, the general appearance of the eruption and the pruritus are suggestive of dermatitis herpetiformis. The failure to have any remissions (she has never gone even so long as a week without active lesions) is a point against the diagnosis as is the lack of grouping. Perhaps these inconsistencies should be overlooked, but it could be a factitious condition.

CAPT IRVING N. HOLTZMAN, M. C., A. U. S. (by invitation) Have you performed a biopsy? Clinically, I do not think that she has dermatitis herpetiformis. She has all the stigmas of a psychoneurotic person. The eruption is generalized, without any grouping, and she has never had any remissions. Unless the diagnosis could be confirmed histologically, I think that the picture is that of neurotic excoriations.

DR HAROLD M. JOHNSON. I thought of that because of her appearance and manner. However, her entire back is covered with either lesions or scars, even in the inaccessible central portion.

CAPT IRVING N. HOLTZMAN, M. C., A. U. S. (by invitation) I think that after ten or twelve years a patient may become expert at reaching the entire back.

CAPT HERBERT LAWRENCE, M. C., A. U. S. I should object to considering her neurotic manner and appearance in the differential diagnosis, because any severely pruritic dermatosis of this duration is likely to induce neurotic characteristics.

#### A Case for Diagnosis (Circumscribed Neurodermatitis?) Presented by CAPT HERBERT LAWRENCE, M. C., A. U. S.

An 8 year old Chinese girl was seen in September 1944, because of a cutaneous lesion on the left cheek, near the nose. This had appeared four years before as a small, scaly, itching macule, which has slowly progressed in size. She has received various types of local treatment and for the last three years has received at sporadic intervals a total of seventeen roentgen ray treatments. At no time has there been any improvement in the appearance of the lesion.

In December 1943 the patient had been seen, complaining of dizzy spells, and after a complete physical examination a diagnosis was made of psychogenic vertigo.

Examination of the skin at this time reveals a sharply circumscribed, lichenified, slightly raised macule about the size and shape of an almond.

#### DISCUSSION

DR HARRY L. ARNOLD JR. I removed a few fragments of scale and found fairly clear evidence of follicular dilatation and plugging. My diagnosis would be discoid lupus erythematosus.

DR HAROLD M. JOHNSON. That was my diagnosis. The lesion has been aggravated by sunlight.

CAPT DAVID MUSMAN, M. C., A. U. S. It does look like lupus erythematosus, but the mother's statement that the lesion occasionally flared up without exposure to sun made me think of a drug eruption or at least of the advisability of excluding that possibility.

CAPT HERBERT LAWRENCE, M C, A U S I almost failed to recognize this lesion today when I saw it It has changed greatly in the one week that she has been using a tar-containing preparation on it Originally, it was a simple lichenified macule, which strongly suggested lichen simplex chronicus

CAPT L H ROSENTHAL, M C, A U S Every one has seen many cases of lichen simplex chronicus, but how many have ever seen one of eruption on the face?

• DR HAROLD M JOHNSON It is certainly rare there, especially on the cheek I think that it would be interesting to see whether this child responds to a series of injections of bismuth

DR HARRY L ARNOLD JR That would be my recommendation, too

CAPT IRVING N HOLTZMAN, M C, A U S (by invitation) I see no objection to trying to confirm the clinical diagnosis by biopsy

### PHILADELPHIA DERMATOLOGICAL SOCIETY

Carmen C Thomas, M D, *Chairman*

Reuben Friedman, M D, *Secretary*

*Dec 15, 1944*

#### Bilateral Matured Cataracts Complicating Atopic Dermatitis Presented by DR MEYER L NIEDELMAN

N G, a white woman aged 28, presents persistent symmetrically distributed dry, scaly excoriated lesions over the face, neck, chest, back, thorax and cubital and popliteal areas and the thighs Some of the areas are exudative The dermatitis first appeared at the age of 5 years It began in the cubital and popliteal areas and spread to the present sites The patient states that she had good vision until one month after the birth of her baby, three months ago, when she noticed dimness of vision, cloudiness and inability to distinguish objects This condition has progressed rapidly until at present she is able to distinguish only light and that faintly The cataracts in both eyes are fully matured Her mother had infantile eczema, and a first cousin, 20 years of age, has eczema

The serologic reaction of the blood for syphilis was negative A urinalysis gave normal results The blood sugar was 82 mg per hundred cubic centimeters A complete blood count revealed 76 per cent hemoglobin, 4,540,000 erythrocytes and 8,500 leukocytes with 59 per cent neutrophils, 28 per cent lymphocytes, 1 per cent monocytes, 11 per cent eosinophils and 1 per cent basophils The patient has had extensive treatment by various methods with little benefit

#### DISCUSSION

DR FRANK C KNOWLES There ought to be an expression of opinion about how frequently this complication is seen in atopic dermatitis It is the first one I have seen, and I think that it is rare Although it is cited as a complication, it is seen so infrequently that to my mind it is a question whether it is a complication or simply a coincidence

DR J M SCHILDKRAUT, Trenton, N J I encountered a similar case, that of a boy with atopic eczema, who had a cataract in one eye which was thought to be a mere coincidence, but I think that such a situation happens too frequently One reads of it in the literature continuously There must be some relation between the eczema and the cataract

DR CARROLL S WRIGHT I tried to find out whether the patient had had roentgen ray therapy, because ophthalmologists sometimes say that roentgen rays

around the eyes may produce cataracts. She said that she had never had anything but ultraviolet rays, but I should like to ask Dr. Niedelman whether she has ever had roentgen rays.

DR MEYER L. NIEDELMAN: No, she has had only ultraviolet rays.

DR CARROLL S. WRIGHT: I have never seen how roentgen rays, in the very small doses used around the eyes, could produce a cataract.

DR SIGMUND S. GREENBAUM: I do not think that this is atopic dermatitis, although it is often called that. I think that the patient's atopy or allergy disappeared a long time ago and what one sees now is the result of an unstable cutaneous nervous system. She has a central (thalamic) feeling of pruritus, and as a result she has a habit of scratching which eventually follows improperly or injudiciously treated cases of atopic or allergic or true infantile eczema. I feel that her skin if left alone would become perfectly normal. Years ago, when cutaneous tests became popular, I did them in many of these cases and found many positive reactions. Then I deliberately prescribed for the patients the foods to which they were supposedly sensitive, but they did not get worse, and when they discontinued those foods, they did not get better.

DR HERBERT J. SMITH: I treated this woman about a year ago when she was pregnant, and her dermatitis cleared up. She had no trouble with her sight at that time and certainly no evidence of cataract. I agree with Dr. Knowles that I have never seen atopic eczema in association with cataract, but from the literature I gather that the conditions occur together in about 10 per cent of cases.

DR SIGMUND S. GREENBAUM: I believe that such cases are few and far between. I agree with Dr. Knowles that the cataract is coincidental, not a complication of the atopic dermatitis.

DR J. M. SCHILDKRAUT, Trenton, N. J.: Some of the ophthalmologists tell me that there is some relationship between eczema and cataract and that it is more frequent now than in the past.

DR MEYER L. NIEDELMAN: The ophthalmologist who referred the patient to me was one of the chiefs at the Wills Hospital for Diseases of the Eye, and he stated that he has seen several similar cases. L. A. Brunsting (*ARCH. DERMAT. & SYPH.* 34:935 [Dec.] 1936) recorded 101 cases, in 10 of which there were cataracts, which seems to me a little high. In most of the reported cases the cataracts were of the juvenile type. Surprisingly, in this woman the cataracts have matured rapidly indeed, so that at present she can barely see light. She will be operated on next week.

#### **Dermatitis Herpetiformis Followed by Lesions Resembling Lichen Planus** Presented by DR. A. G. PRATT

B. G., a white woman aged 23, presented grouped vesicular lesions of various sizes on the legs, arms and trunk on admission to the hospital. These rapidly dried and were followed by lesions suggesting lichen planus, especially on the extremities. There was no outbreak on the head. (Since the foregoing statement was written, vesicles have reappeared.) Twenty months ago red macules followed by vesicles appeared on the feet and spread to the arms and trunk. Itching was severe. After treatment by local physicians the patient entered the hospital in February 1944 and in two weeks was discharged free of all traces of any cutaneous disorder. The vesicles had rapidly disappeared and were succeeded by flat purplish shiny lichenoid lesions, which in turn disappeared. A month later there was a relapse. Vesicular and bullous lesions again appeared. Under her upper plate on the soft palate a bulla developed, followed by superficial erosion. The patient is a well nourished woman, the mother of two children, the last of whom was born just before the cutaneous trouble started. Her general health is good. The upper jaw is edentulous. The heart and lungs are normal, as are the temperature, pulse and

respiration The tonsils are much enlarged and partly covered with a whitish exudate

Studies of the blood revealed normal conditions, except for a leukocyte count of 16,500 on two occasions The Wassermann and Kahn reactions of the blood for syphilis, on Feb 19, 1944, were negative On November 30, the Wassermann reaction was again negative A roentgenogram of the chest showed no tuberculosis

On the patient's first admission to the hospital, in February 1944, she was given only solution of potassium arsenite U S P by mouth On her admission on November 24, she received sulfadiazine and sodium bicarbonate, 1 Gm of each every four hours for twelve days Solution of potassium arsenite in ascending doses to 5 minims (0.31 cc) three times a day was also administered

#### DISCUSSION

DR BERTRAM SHAFFER I suggest that this eruption may be a bullous lichen planus

DR FRED D WEIDMAN I understand that at the hospital, with a galaxy of experienced dermatologists, it was agreed that this was a classic case of dermatitis herpetiformis It seems to me tonight that this is not lichen planus but only a lichenoid eruption I think that this case was primarily one of a circinate eruption of dermatitis herpetiformis with clearing in the center and that it is the acuteness of the processes around the vesicles which has led to a larger amount of inflammatory residuum than is usually seen in cases of dermatitis herpetiformis and that the papules that are now seen represent an inflammatory residuum of the dermatitis herpetiformis The eruption has the distribution of erythema multiforme, I have long thought that dermatitis herpetiformis in the final analysis, (that is, from the standpoint of pathologic processes) is of the order of an erythema multiforme That would tie in with this case and account for the distribution of the peripheral papular features

DR ISADORE ZUGERMAN I agree with Dr Weidman that if this eruption were lichen planus one should expect to find lichen planus lesions elsewhere than in areas where the bullous lesions were previously found It does not seem that this has occurred Solution of potassium arsenite and sulfonamide compounds may originate bullous eruptions in some cutaneous diseases Erythema multiforme could have been the original form of this disease, with sulfadiazine and the arsenic originating and continuing the bullous lesions

DR FRED D WEIDMAN I suggest in cases like this that investigations be made for focal infections One of my patients for whom Dr Schamberg and others had made a diagnosis of dermatitis herpetiformis was found at necropsy to have had suppurative bronchiectasis, which had escaped diagnosis That is, there was a focus of infection which had been operating in the patient for years

DR CARMEN C THOMAS There is a note that the tonsils are much enlarged and partly covered with a whitish exudate

**Parapsoriasis Varioliformis** Presented by DR HENRY B DECKER

P R, a white youth aged 18 years, had an eruption in March 1944 which was diagnosed as varicella He suffered a recurrence in October 1944

#### DISCUSSION

DR HERMAN BEERMAN I consider this a case of Mucha-Habermann's disease It is the first to be presented here in several years

DR CARMEN C THOMAS What have the members found most effective in the treatment? This patient has had no treatment

DR SIGMUND S GREENBAUM Time

DR HERMAN BEERMAN In 1 case, time and ultraviolet rays helped the patient

DR FRANK C KNOWLES I think that the term "parapsoriasis" is unfortunate In the past it was practically a dumping ground for almost every disease of the

skin, whether dry or moist, which one did not know exactly where to place. Such a group disease one puts under the heading of parapsoriasis, without any effort to find an appropriate term to describe the lesions. To my mind to place dry, vesicular and pustular eruptions under the one heading is unfortunate. I think that parapsoriasis should be limited to a special entity.

**Fixed Eruption (Arsenic, Bismuth?)** Presented by DR BERNARD L. KAHN

I S., a Negro woman aged 22, presents a multiform macular circinate eruption of the face and body. She received antisyphilitic therapy when she had secondary syphilis. The last course of the bismuth compound was completed May 4, 1944, and the last course of oxophenarsine hydrochloride (mapharsen) was completed on November 30. After forty-two doses of bismuth subsalicylate and forty-four of arsenicals, a fixed eruption developed over the face and body. She has not yet received treatment for the eruption.

The serologic reaction of the blood for syphilis was negative on Nov. 30, 1944. The spinal fluid was negative for syphilis on Nov. 22, 1943. A complete blood count was essentially normal.

DISCUSSION

DR FRANK C. KNOWLES: I think that this is not an eruption due to bismuth. Inasmuch as this woman has been taking an arsenical as well as a bismuth preparation, the eruption should be regarded as of arsenical origin rather than as due to bismuth. I believe that bismuth does not give rise to any fixed types of eruption. This patient presents no involvement of the mucous membranes and no pigmentation such as often is caused by bismuth.

DR HERMAN BEERMAN: I have yet to see a real fixed eruption which could be proved to be due to bismuth, but I have seen such an eruption in patients who have received bismuth, though whether or not it was due to bismuth, I do not know. According to Dr. Abramowitz and others, almost anything will produce a fixed eruption. They even speak of a drugless fixed drug eruption. They speak of a fixed eruption due to magnesia magma. If that can produce it, I see no reason why bismuth cannot.

DR FRANK C. KNOWLES: I do not think that one should attribute an eruption on the skin to any one drug if more than one drug is being taken. As long as one knows that fixed eruptions may be present over a period of months, it does not follow that the drug being taken at the present time is the cause; the eruption may be due to a drug that was taken immediately previously.

DR LOUIS GOLDSTEIN: I think that a simple test would be to give the patient a rest and then give an arsenical and a bismuth compound separately and see which aggravates the eruption.

DR HERMAN BEERMAN: Recently I saw a man who in 1937 had a bullous eruption which subsequently became pigmented. Not long ago, he took phenolphthalein and reappeared on account of a new eruption. It was definitely shown that he had taken phenolphthalein, and in a short time he died. Fatal results from drug eruptions must be kept in mind when one is considering proof of the cause of the eruption by readministering the suspected preparation.

**A Case for Diagnosis (Scleroderma, Atrophoderma, Acrodermatitis Atrophicans Chronica?)** Presented by DR J. M. SCHILDKRAUT, Trenton, N. J.

M. F. R., a white woman aged 40, of good general appearance, presents on the anterior surface of the left thigh a palm-sized area, ivory colored and hard on palpation. A similar patch is present on the dorsum of the left foot. In addition, the skin of the thigh and leg is thin, atrophic, dusky red and scaly, and these conditions extend over the lower portion of the abdomen. There is also pain in the left leg. The hardened areas are softening, but the atrophic condition is spreading. The dermatosis began in July 1943.

## DISCUSSION

DR SIGMUND S GREENBAUM One observes sclerodermatous lesions in acrodermatitis atrophicans chronica as well as calcified and fibrous nodules

DR FRED D WEIDMAN Morphea really fits the case better One might try bismuth subsalicylate, which Dr Klauder has been employing after a lead by Dr Stokes

DR J M SCHILDKRAUT, Trenton, N J The patient has been treated with a neostigmine salt I think that the lesions are somewhat softer Associated with the atrophy there is a quasi-ichthyotic condition, for which I gave her vitamin A She complains of severe pain in the leg I have also given her estrone How is the bismuth compound given?

DR HERMAN BEERMAN In the same way as bismuth subsalicylate Dr Stokes spoke of a French report which concerned bismuth hydroxide, but Dr Klauder's case illustrates the fact that one may use other bismuth compounds, apparently it is the bismuth that effects the improvement

DR CARMEN C THOMAS This patient complains of considerable pain from the cold of the floor, and I wonder whether the pain is not due to vasospasm

## NEW YORK DERMATOLOGICAL SOCIETY

Hans J Schwartz, M D, *President*

George C Andrews, M D, *Secretary*

*Dec 19, 1944*

**A Case for Diagnosis (Pigmentation of Lip and Buccal Mucosa) Presented by DR JOHN C GRAHAM**

Mrs I R, 51 years, is a graduate nurse About two years ago she first noticed a pigmented spot on the right side of the lower lip, inside the vermilion border Similar spots have spread gradually to involve other parts of the mucosa of the lower lip and the buccal mucosa of both cheeks to some extent There have been no subjective symptoms Neither has there been any history of drugs applied locally or taken internally

The pigmented areas are not indurated, and they appear normal in every way except for the deposit of pigment, which is increasing in extent The individual patches are not getting darker The principal complaint is the disfigurement

## DISCUSSION

DR A BENSON CANNON For many years I have frequently observed patients with such brown pigmented spots on the mucous membranes of the lips and mouth, most of these patients giving a history of having received arsenic The pigmentation is superficial, and I have successfully removed the areas by lightly desiccating them with the electric needle Several years ago Dr Pusey reported similar cases (ARCH DERMAT & SYPH **36** 613 [Sept] 1937) in his article on pigmented spots of the mucous surface of the lips I think that the blood and the urine should be examined for arsenic If the patient objects to the appearance of the pigmented spots, they can always be removed with the electric needle

DR MAURICE J COSTELLO I have seen this type of pigmentation on several occasions following bismuth therapy

DR GEORGE M MACKEE I have been interested in this pigmentation as occurring in the mouth, the vagina and the anal mucosa While some might be due to heavy metal or arsenic retention, I am more inclined to think of a nevus defect or a rudimentary pigmentation In this connection, the skin and the mucous membranes of many mammals are heavily pigmented

DR JOHN C GRAHAM To the best of my knowledge, this patient has had no heavy metals. She is intelligent, and close questioning has not brought out any history of any heavy metals. She may have received arsenic from some extraneous source. She lives on the eastern end of Long Island, where large quantities of potatoes are raised. In potato culture large quantities of arsenic are used, and it may be possible that over the years the patient has absorbed arsenic from the dust in the air. Other than that, I cannot possibly account for it.

#### A Case for Diagnosis (Tuberculoderma?) Presented by DR FRED WISE

P I, a girl aged 14 years, was referred by Dr T W Baer, of Pittsburgh.

At the age of 5 years she had scarlet fever, and shortly after this subsided what appeared to be a papular rash developed. As this eruption subsided, it left bluish, atrophic discolorations on her arms and legs. During the fall of 1940 she had chorea. In March 1942 she had rheumatic fever. This was followed by severe pains in the calves of both legs and the shortening of the achilles tendon of each leg. In September 1942, during her hospitalization, the Kahn reaction of the blood was negative. Spinal fluid examination gave the following findings: the cell count was 1, the globulin reaction was negative, the Wassermann reaction was negative, and the colloidal gold curve was 000000000. The basal metabolic rate was -2 per cent. A roentgenogram of the bones revealed the sella turcica as normal, as were the bones of the legs. A roentgenogram of the chest showed no abnormality.

On Sept 15, 1942, a biopsy of the skin from the left calf was taken, with the patient under anesthesia with procaine hydrochloride, the section did not reveal any definite findings. On September 22, tenotomy of the achilles tendons was performed. Subsequently, with the finding of an endocarditis, a tonsillectomy was performed and it resulted in apparent clearing of the clinical cardiac findings.

The patient was under the observation of Dr Baer since Oct 7, 1944, at which time she presented large ulcerations on the extensor surfaces of both legs. These ulcerations would increase in size, heal in one area and break down in another, until final healing of the involved sites occurred after five weeks.

On Nov 24, 1944, the patient reported that while sitting in school on November 22 she felt a burning sensation over the extensor surfaces of both arms and legs, and, on examination, fresh lesions were found on these areas. The lesions appeared as erythematous patches on the extensor surfaces of her arms and legs. The areas quickly formed what seemed to be iris type lesions. The central portions became bullas, which were filled with viscous, hemorrhagic material. After the overlying skin was drained, the resulting lesion was a moderately deep ulcer.

The patient received  $\frac{1}{4}$  unit of unfiltered roentgen rays to all the involved sites at each office visit. She has been given weekly injections of crude liver extract. Oral medication consisted of the following: mixed vitamins and, from November 24 to December 9, sulfadiazine tablets, 77 grains (49 Gm), taken four times a day. From December 9 to the time of this presentation she has taken the sulfadiazine twice daily.

#### DISCUSSION

DR GEORGE M MACKEE I cannot make a diagnosis but lean definitely to some type of tuberculosis or tuberculid. I saw one elementary lesion which was a small, deep-seated nodule.

DR GEORGE C ANDREWS I agree with Dr MacKee. I feel that the lesions on both the legs and the arms look like tuberculids.

DR MAURICE J COSTELLO I agree with the previous speakers. More specifically, I believe that she has tuberculous gummas independent of underlying tuberculous foci. I also noticed a peculiar atrophy of the cheeks, which I believe is associated with the other lesions.

DR A BENSON CANNON I suspect that the lesions are self induced. I have never seen a dermatologic disease similar to the lesions present in this case, nor



have any of the former investigators been able to make a diagnosis clinically or from their laboratory investigations. The child has spent most of her life in various hospitals and has the background (psychologically) for self induced lesions. The ulcers are certainly traumatic in type. Her actions and facial expression as she entered the room caused me to suspect that she might be a malingerer. I believe that if a plaster cast were put on the extremity all the lesions would heal.

DR FRED WISE. The patient had been previously presented before several dermatologic groups in Pittsburgh, but no definite diagnosis had been established. I am in agreement with the opinions expressed by other members that the eruption is in all probability a form of tuberculosis or tuberculid, but I am unable to reconcile such a diagnosis with the extensive scarring on the skin of the knees. I regret that Dr Cannon's suggestion as to diagnosis does not appeal to me in this instance.

DR GEORGE M. MACKEE. I agree with Dr Wise that this is not a self induced eruption. There are innumerable papules on each cheek and atrophy. Another interesting feature is the eruption around the elbows and knees.

### **Xanthoma Tuberosum, Keloid, Jacquet Posterosive Syphiloid** Presented by DR. GEORGE M. LEWIS

J. H., a 4 month old infant, was first seen on Dec 1, 1944 at the skin clinic of the New York Hospital. According to the mother, three weeks after birth several reddish yellow lesions appeared in the inguinocrural region. This was followed by the appearance of similar elevations on the scalp and trunk about two weeks later. Since that time, no new lesions have appeared and the old ones have remained stationary. In both inguinocrural folds there was diffuse erythema. On the right side of the vulva and on the right buttock are round, reddish yellow, slightly eroded nodules, about 3 by 2 cm., under the left costal margin, and in the right parietal region are firm, yellowish red papules about 1 by 2 cm. The blood from the cord gave a negative serologic reaction. A dark field examination from an eroded lesion was negative. The mother's blood gave a negative reaction to the Wassermann test.

#### DISCUSSION

DR MAURICE J. COSTELLO. Lesions occurring in the diaper region have been described as similar to condylomas, and I believe that these are pyogenic lesions simulating condylomas.

DR GEORGE C. ANDREWS. I was impressed by the yellow, lemon color of the lesions of the scalp and believe that they are juvenile xanthomas and that the other lesions will become yellowish. If this is true, it is better not to treat them. I have had 2 cases in which juvenile xanthoma disappeared when the children reached 4 or 5 years of age. Some patients have been helped by thyroid extract.

DR GEORGE M. MACKEE. I agree with Dr Andrews.

DR FRED WISE. I agree with Dr Andrews also. I have an idea that fibroxanthoma is being dealt with. McDonagh described similar cases, and I think that it is possible that these lesions might turn out to be xanthoendothelioma. I suggest that a biopsy may offer additional evidence.

DR A. BENSON CANNON. I should first attempt to rule out bromides as the cause. I have seen several cases of infants born with bromide tumors that were identical to this and I should think that an estimation of bromide in the blood and the urine should be made.

DR FRANK C. COMBES. I agree with Dr Wise. McDonagh called these nevoxanthoendothelioma. They are probably neither nevi nor endotheliomas although they are xanthomatous.

DR FREDERICK REISS (by invitation). At the time the child was presented, the lesion in the inguinal region looked suggestive of posterosive syphiloid, but in the past few weeks the condition has definitely changed and the lesions in the inguinal

region are similar to those in the occipital and parietal region. I think that this is possibly a case of xanthoma or neuroxanthoendothelioma.

#### **A Case for Diagnosis (Sarcoid, Leprosy?) Presented by DR FRED WISL**

Mrs P. L., a married woman aged 49 years and a native of Nassau, West Indies, was under the care of Dr. Francis Pascher, of Brooklyn. The patient had a generalized macular, nodular and tuberculous eruption, which first appeared about ten years previously. She had lived in this country since childhood.

Her history indicated that she had been hospitalized for a period of seven weeks and that a diagnosis of Hodgkin's disease (lymphogranulomatosis) was made in 1935, based on two biopsy examinations. She received daily roentgen ray treatments for ten days while in the hospital.

In the past two years, Dr. Pascher's investigations revealed the following findings: a biopsy of a nodular lesion on the abdomen showed the characteristic changes of Boeck's sarcoid, a roentgenogram of the lungs was normal, examination of the hands on Jan. 4, 1943, showed changes suggestive of rarefaction of the head of the proximal phalanx of the first finger of the right hand and the head of the second metacarpal bone, the Wassermann reaction of the blood was negative, and quantitative tests with tuberculin showed an anergic response.

On presentation, examination showed a widespread eruption involving the head, face, trunk and extremities. The lesions were most abundant on the back and extremities, they consisted of flat plaques, nodules and tumefactions of reddish brown and coffee color, on the wrists, the individual lesions were tuberculous and most prominent. The outer aspects of the eyebrows were devoid of hair, the cervical lymph nodes on the right side of the neck were enlarged, there was a moderate grade of interosseous atrophy of the knuckles of the hands but no evidence of thickening of the palpable nerve strands. Tests for presence of anesthesia of the skin were negative. (Tests for heat and cold sensation were not reported at the time of presentation.) Search for the microbacillus of leprosy was fruitless. The patient had lost about 20 pounds (9.1 Kg.) in the past two years.

Unfiltered roentgen ray therapy combined with subcutaneous administration of arsenic, given two years previously, had resulted in complete resolution of the cutaneous lesions, with the exception of the tuberculous lesions on the wrists. The present attack, however, has failed to respond to roentgen therapy.

#### **DISCUSSION**

DR. GEORGE M. MACKERR: This may be a case of leprosy, but this is such a serious diagnosis that it is necessary to prove it by finding the bacillus of Hansen and also by ruling out sarcoidosis. The eruption shows hyperesthesia instead of hypoaesthesia. The persistent pruritus may be merely an essential pruritus.

DR. GEORGE C. ANDREWS: Every once in a while a disease is seen which is extremely difficult to diagnose. This looks like leprosy, yet it may turn out to be sarcoid. A diagnosis should not be made until the histologic report is received.

DR. GERALD F. MACHACEK: I saw this woman about eight years ago at the Roosevelt Hospital. Although I suspected leprosy at the time, I assumed that she had not been to the West Indies. The outstanding symptoms were intense pruritus and glandular swelling. She presented only an occasional lesion on the abdomen and thighs. A lymph node was removed, from the sections of which a diagnosis of Hodgkin's disease was made. I saw sections from the abdominal cutaneous lesions and, suspecting leprosy, stained some by Ziehl-Neelsen's technic but discovered no bacilli and finally concluded that the lesion was a lymphoblastic infiltration with tuberculoid structure, particularly as there were not many epithelioid cells present. Although pruritus continued to be the outstanding complaint, the signs of nerve involvement have since developed. Last month the patient noticed a foot drop of the right extremity. She has had ulcerations but no nerve symptoms except hyperesthesia or pruritus. Her case must be reevaluated. It is probably

leprosy, but there is a remote possibility of a tuberculoid lymphoblastoma involving the nerves

DR MAURICE J COSTELLO The features presented in this case favor both leprosy and sarcoid I should favor the latter diagnosis because of the patient's failure to react to the intradermal injections of tuberculin The foot drop may be due to some bony changes in the sacrum, with indirect pressure on the lumbosacral region

DR FREDERICK REISS (by invitation) There are certain features of leprosy which I should want to correlate with this eruption The clinical features, especially the nodules, are suggestive of leprosy, but the histologic changes, as interpreted by Dr Sims, would be a contraindication in such extensive formation of nodules In tuberculoid leprosy, the sensory changes would be more prevalent than they are in this case As Dr MacKee pointed out, there is more or less hyperalgesia That would not be in accordance with what is known of tuberculoid leprosy Changes in the bone could, of course, occur in tuberculoid leprosy, but without corresponding clinical findings I think that it would be rather difficult to entertain this diagnosis Moreover, if this is the nodular type of leprosy, sensory changes could be absent, and in that case an entirely different picture would be expected, in addition, leprosy bacilli would be easy to find

DR FRANK C COMBES I agree with everything Dr Reiss has said There is not a tremendous difference in the biologic actions associated with sarcoid and the tubercular type of leprosy, blood changes and bony changes are similar, although there are certain distinguishing features I should spend all my time in this case looking for Hansen's bacillus

DR A BENSON CANNON I am convinced that the patient has leprosy I have seen patients with leprosy with just as many lesions as this patient has, and the enlargement of the lips, lobes of the ears, eyebrows, wrinkling of the forehead, the brownish red, soft tumors, the large ulnar nerves and the foot drop are all characteristic symptoms of leprosy Itching and hyperesthesia are common symptoms in nodular leprosy Dr Kellersberger, of the American Mission to Leprosy, in a personal communication, stated that Pron, a new sulfur derivative, has given the greatest hope of success in the treatment of leprosy of any remedy yet used He stated that Pron has been in use at the leprosy colony in Carville, La, for the past few years and has proved to be beneficial in the treatment of certain types of the disease Pron should be of benefit in this type of leprosy I feel reasonably certain that if careful search is made for Hansen's bacilli they will be found

DR GEORGE C ANDREWS I have corresponded recently with Dr Guy H Faget, in charge of the United States Marine Hospital (National Leprosarium) in Carville, La, concerning the use of Diasone (disodium formaldehyde sulfoxylate diaminodiphenylsulfone) and Promin He stated that the results of treatment with Diasone thus far are similar to those obtained with Promin, which has an inhibitory action on the progress of the disease Although he has been using these drugs for about five years, it is still too early to form any definite opinion as to their mode of action and their limitations in such a chronic disease as leprosy The action is slow, and benefits do not become manifest until after six months of therapy Benefits are shown more rapidly with Diasone than with Promin, but, on the other hand, the ulcerative complications, keratitis and laryngitis, do not respond so readily

DR MAURICE J COSTELLO The patient has lesions on the scalp, which is extremely unusual in leprosy Have roentgenograms of the lungs been taken?

**Sycosis Vulgaris (of Ten Years' Duration)** Presented by DR HOWARD FOX

P J G, aged 33, a truck driver of Italian extraction, has suffered from an eruption of the bearded region for the past ten years At the onset, the patient said there were individual pustules, which eventually changed to the present type of eruption

He now presents a dry, scaly eruption involving the entire surface of the bearded area and that of the upper lip. He is an intelligent man and is apparently a cooperative patient.

He has been treated by other physicians, with many remedies, but without permanent effect. He said that the best results were obtained from a dozen weekly treatments with roentgen rays. At no time were roentgen rays used to cause epilation. Other methods of treatment included ultraviolet irradiation, mechanical epilation by "Zip" methods, staphylococcal vaccines, ammoniated mercury ointment, boric acid ointment, gentian violet medicinal, penicillin given intramuscularly (total of 1,000,000 units) and compound chlorohydroxyquinoline ointment, which he has used daily for a year. He has had no sulfonamide drugs. The eruption is only partially improved by chlorohydroxyquinoline ointment.

The patient is presented for therapeutic suggestions.

#### DISCUSSION

DR GEORGE C ANDREWS. I should suggest the use of sulfadiazine internally.

DR GEORGE M. MACKEE. Recently I have had several patients with sycosis vulgaris of twenty years' duration. The lesions had resisted all conventional therapy, including sulfanilamide drugs, roentgen rays and penicillin by injection but cleared up in a few weeks with penicillin ointment, 500 Harvard units to the gram. The vehicle seems to make little difference. I have used Aquaphor hydrous wool fat and modern greaseless creams as vehicles, with equally good results.

DR GEORGE C ANDREWS. I have had similar results with penicillin ointment, using different bases, in a strength of 500 units. It certainly gives remarkable results in sycosis vulgaris.

DR GEORGE M. LEWIS. A patient has been hospitalized at the New York Hospital who had sycosis incidentally, and when penicillin was administered for another disease the sycosis promptly responded. I am still waiting for the eruption to return. It is now well over a month, and the condition has not yet relapsed.

#### Hemangiopericytoma. Presented by DR. FRANK WISE

P. C., a boy aged 4, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on July 18, 1944, presenting a growth on the nose, of one year's duration. It began as a pinhead-sized node, which gradually enlarged to its present size.

On the base of the columella of the nose is a pea-sized, smooth, firm growth, red and well defined, resembling an angioma.

Histologic section examined by Dr. Charles F. Sims was diagnosed as hemangiopericytoma. The description is as follows: "Throughout the upper, middle and deep corium is a diffuse and ill defined cellular mass. Throughout this mass one may note many dilated vessels, with lumens of varying size. Surrounding these vessels and fusing with those of neighboring vessels are many spindle-shaped cells with rather large round or oval hyperchromatic nuclei and poorly defined cytoplasm."

#### DISCUSSION

DR. GERALD J. MACHACEK. By pericytoma the pathologist means a tumor composed of cells found in the walls of blood vessels. Morphologically, this tumor is composed of spindle cells and is probably benign.

DR. GEORGE C. ANDREWS. There was a tumor precisely like this on the chin, described by Stout, under the title of "angiopericytoma" with microscopic features which, of course, are just the opposite of those of hemangioendothelioma. Whereas the latter arises from the endothelium, this tumor arises from the adventitia of the blood vessel. Like the hemangioendotheliomas in children, they are benign.

DR. GEORGE M. MACKEE. I saw this section only under low power, and it is my impression that the infiltrating cells are fibroblasts. I wonder whether it might

not be an angiofibroma I recommend excision or leaving it alone There is too much fibrous tissue formation for the use of radium

**A Case for Diagnosis (Lichen Chronicus Simplex with Nodular Growths)**  
Presented by DR FRED WISE

J B, a white woman aged 29, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Sept 12, 1944, presenting lesions on the hands since 7 years of age Her twin sister is not so affected The patient had infantile eczema of the scalp and face at 8 months At 7 years she had dry, scaly patches in the cubital areas She complains of some itching, worse when oozing Her state of health has been good

The eruption began as a rough, itchy and scaly patch on the dorsal surface of the right little finger At 12 years the middle finger of the right hand, at 13 the rest of that hand and at 14 the left hand became similarly affected This eruption sometimes partially regressed, but it recurred She received roentgen ray treatments since 1930 to the dorsal and palmar surfaces of the hands and the cubital and popliteal regions, but more to the hands, every two weeks at irregular intervals for a period of two years In 1932 she was treated with ultraviolet and carbon arc exposures and, later, with injections in the scapular region In 1937 a match-head-sized growth first appeared on the dorsal surface of the right middle finger Within a few months others developed on the same finger They gradually appeared on the dorsal surface of the right hand during the succeeding seven years Some months later similar lesions appeared on the left hand For the past two years the patient has been having "heart burn and gas" Gastric analysis and a hemogram in January 1945 were said to be normal The eruptions on her hands became aggravated after she ate chocolate and too much meat, fish and cheese The patient stated that for the past two months she has noticed that if she stays on a diet with a low phosphorus content and takes calcium phosphate, calcium gluconate and vitamin D wafers three times daily the oozing stops and her hands "would be better"

On the dorsal surfaces of the hands, fingers and wrists are fairly well defined, hard, hemispherical white nodules, isolated and closely grouped, varying from the size of pinheads to that of matchheads and split peas They are painless, raised, smooth and symmetrically distributed, mostly on the dorsal surfaces of the hands and wrists The skin of the entire dorsal surfaces of the hands, fingers and wrists is thickened, less elastic, moderately infiltrated and covered with ill defined scaly patches There are numerous fissures, most pronounced on the knuckles The palmar surfaces are comparatively free except for some fissuring and crusting in the creases There are lichenified patches and eczematized, fairly well margined patches in the cubital and popliteal areas, with exaggerated markings on the skin, fissuring and crusting on erythematous bases and mild lichenified patches on the neck On diascopic pressure the nodular growths are partially compressed, revealing uniform white spots Atrophy and telangiectasia were not present

The urine was normal The hemogram was normal except for 4 monocytes and 8 polymorphonuclear eosinophils

Two nodules were excised and examined histologically by Dr Charles F Sims The interpretation is as follows "The epidermis is moderately and fairly regularly acanthotic Throughout the upper corium and midcorium is a diffuse cellular reaction, composed of rather large cells with poorly defined cytoplasm Between these cells the collagen has undergone a degeneration which suggests the edematous and granular type Many fibroblasts are scattered throughout the zone The findings suggest a degenerative process which cannot be placed in a definite category While some of the features are in part suggestive of granuloma annulare, they are by no means definite"

DISCUSSION

DR JOHN C GRAHAM I never heard of such lesions ascribed to roentgen rays I have no idea what they are

DR FRANK C COMBES I do not think that these lesions are related to the roentgen therapy that this patient has had. They struck me as being part of the lichenification. She has a great many along the arm, and these impressed me as being lichenized lymphedema.

DR GEORGE M MACKEE The patient apparently has neurodermatitis. The interesting feature is the large papules or nodules. It is possible that these lesions are the result of years of rubbing and scratching and may be nothing but exaggerated lichenification or hypertrophic papules. However, this is not borne out by the histology. I have not seen lesions of this sort before in neurodermatitis. It may be that she might have these lesions even if she did not have neurodermatitis. They resemble the lesions seen in elderly or old people, especially those who have had long, continued exposure to solar rays, in other words, keratosis. This is suggested also by the histology. It is a degenerative process.

DR PAUL E BICHERT I have not infrequently observed papules aggregated in patches, with scaling and much thickening of the skin, apparently entirely caused by friction. In one particular instance, in a woman patient, a similar clinical picture was produced by daily friction with a pumice stone for several consecutive years in attempts at removing superfluous hair.

DR FRED WISE I am glad to learn that none of the members regard this eruption on the hands as a roentgen ray effect just because there is a history of exposures to roentgen rays for the associated atopic dermatitis. The nodular lesions closely resemble the nodular neurodermatitis described by Kreibich.

#### **A Case for Diagnosis (Bowen's Disease?) Presented by DR ANTHONY C CIPOLLARO**

L. P., a Puerto Rican woman aged 64, first attended the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in the service of Dr. Williams in 1935. About twenty years ago she had a lesion in the perianal area, which was treated with roentgen rays in Puerto Rico. The disease improved but later recurred. When the patient attended the Skin and Cancer Unit, several biopsies were made. One of them showed the lesion to be that of Bowen's disease, and another showed it to be a possible prickle cell epithelioma. The patient was referred to the surgical department, where most of the involved tissue was removed and skin grafts were performed. A proctoscopic examination showed no involvement of the rectum.

This patient was previously presented at the New York Academy of Medicine, Section of Dermatology and Syphilis, on Nov. 6, 1944 by Dr. Eugene Traub.

The patient now presents a lesion affecting the perianal area, which is oval in shape and measures in its greatest diameter about 10 cm. It is elevated and the surface is cauliflower shaped and granulomatous. Along the edges of the lesion there is some hyperkeratosis. There is no definite pearly border and no definite ulcer formation. The clinical appearance of the lesion is that of a granuloma.

#### **DISCUSSION**

DR GERRIT J. MACHACK The two slides which Dr. Cipollaro presented differed. One was definitely that of Bowen's disease, and the other was that of an epithelioma forming what appeared to be incomplete epidermal appendages invading the corium. The lesion was evidently Bowen's disease which had become transformed into a classic epithelioma.

DR GEORGE C. ANDREWS This is an interesting and unusual case. Bowen's disease does sometimes metastasize, and this lesion may be such.

DR RAY H. RULISON This is an interesting case. The disease process is much more advanced than I have ever seen in the past in similar cases.

DR FRANK C. COMBES I agree with the diagnosis as presented. One purpose of this presentation was suggestions as to therapy. The only therapy I can conceive

of is excision and further plastic operation I should like to ask whether the invasiveness of the lesion increases its radiosensitivity?

DR ANTHONY C CIPOLLARO I am glad that Dr Machacek confirmed the histologic opinions previously given. This patient looked like this prior to her operation in 1935. During the past nine years the disease has been slowly progressive, and there is no evidence of metastasis. I wonder whether irradiation might not be the proper approach at the present time? I am aware of the fact that Bowen's disease is not particularly radiosensitive.

#### Extensive Lupus Vulgaris Presented by DR FRED WISE

K K, a Polish working woman aged 54, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec 5, 1944, presenting lesions of fourteen years' duration. She has been in good general health continuously. She has three sons, the oldest 25, living and healthy. One child died of pneumonia at 4 years.

The patient presents an extensive eruption on the face, neck, trunk and extremities. The lesions are dull, yellow-red, rough, painless, nontender and covered with adherent sparse scaling and some crusting. The eruption involves two thirds of the right side of the forehead, both cheeks, the right ear and the retroauricular region and the entire midface, including the nasal mucosa, except for the left ala nasi and the central two thirds of the chin. This eruption is continued uninterruptedly downward, to envelop, except for a 5 cm area on the left side, the entire neck, ending in a well margined border curving upward from the manubrium along the infraclavicular lines. There is a total of eight oval and round isolated lesions on the back, varying from 1 to 3 cm in diameter, and six lesions on the extensor surfaces of the elbows and arms. There is a 7 by 10 cm growth located on the left cubital region. On the vertex of the scalp is a fairly superficial half-dollar-sized scaly patch.

The lesions on the forehead and right cheek are irregular, because of ill defined nodular growths, most prominent at the borders. They are superficial and evenly distributed along the neck and V area of the chest. The lesions on the trunk and extremities are round and oval, with well delimited borders rising straight above the skin, 2 to 4 mm in height. The exaggerated ridges and furrows run upward from the raised edges and converge in the center of the shallowed surfaces. They thus resemble closely, except for the color, the appearance of evenly flattened and hollowed dried figs.

A section was examined histologically by Dr Charles F Sims. It was diagnosed as lupus vulgaris. The description follows: "The epidermis is somewhat thinned, with flattened rete pegs and corresponding papillary bodies. Throughout the upper corium and midcorium are scattered groups of epithelioid and giant cells surrounded by a moderate cellular infiltration composed of small, round and wandering connective tissue cells."

#### DISCUSSION

DR GERALD F MACHACEK Isolated cases of lupus vulgaris respond to various types of therapy. I have seen a patient with lupus vulgaris benefited by local injection of chaulmoogra oil. A good many years ago, in spite of Finsen therapy, I saw the best results obtained at the Vienna *Lupus Heilstatte*, resulting from local excision of small lesions. Repeated focal electrodesiccation has also yielded results. In other words, methods which set up local inflammations or result in complete destruction may be successful. In the English literature there are reports of the successful use of injections of starch locally.

DR MAURICE J COSTELLO I tried the method of injections of starch solutions on several patients with lupus vulgaris, with poor results. My suggestion would be to have the patient try to follow a salt-free diet. Otherwise the patient should be left alone. Occasionally, generalized ultraviolet irradiation might be of some help in conjunction with local therapy.

DR PAUL E. BRCHLT I also believe that local destruction in such an extensive eruption is contraindicated. Perhaps a salt-free diet rigidly carried out might prove of some benefit, though my personal experience with it has not been encouraging.

DR ANTHONY C. CIPOLLARO The methods of treating lupus vulgaris are not satisfactory. In an extensive eruption such as this, hospitalization and rest in bed, an adequate high vitamin diet, generalized and localized ultraviolet irradiation, tuberculin injections and all other methods which would improve the general health should have favorable results.

DR FRANK C. COMBES I agree with Dr Cipollaro in regard to local treatment. I do not think that it is of any value in patients with lupus vulgaris if they are not amenable to plastic surgery. I should like to see a patient treated with either Promin or Diasone, treatment such as was suggested today in the case of leprosy. I am anxious to see what the results would be.

DR FRED WISE While one might argue that in view of the age and apparent good health of the patient it might be best to refrain from treating these extensive lesions, I fear that the patient would merely become a "shopper" from one clinic to another. I believe that attempts at improving the eruption with skin grafts, plastic operation and graded injections of old tuberculin should be made.

#### **Erythema Multiforme** Presented by DR FRED WISE

N. P., a barber aged 47, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Sept. 5, 1944, presenting generalized lesions of four months' duration. He gives a history of sunburn. The day after the sunburn he had chills which lasted for a few hours. Three or four days later a rash with "blisters but no fluid in them" appeared. It itched severely the first two weeks of the eruption. Since then the itching has been slight and only in the lower limbs. He stated that he has been a heavy drinker. He gave no history of ingesting any drugs except acetylsalicylic acid for headaches. He did not remember ever having been sick.

The eruption begins as pea-sized patches and within a few weeks the diameters of some vary in size from that of a cherry to that of a quarter. They then dry and clear in the center, forming a ring. Some remain as such, while others form larger rings. Some lesions last a month breaking up and leaving irregular spots, while others have persisted since inception. There were lesions in the mouth about two months ago. The patches that have regressed have been mostly on the back, only a few being on the extremities.

The lesions are generalized, symmetric and profuse and are located mostly on the extremities, including the dorsal surfaces of the hands and wrists, the mid-abdomen, the buttocks, the knees and the genitalia. The back, except for the scapular regions, is free, the brownish residual spots still being fairly clearly discernible as the site of the former patches. There are patches on the lower eyelids. The diameter of the lesions ranges from that of a pea to that of a silver dollar and larger. Some, the smaller patches, are round, others are ring shaped or oval shaped, with broad borders. There are larger serpiginous and bizarre-shaped patches due to coalescence of the broken-up ringed lesions. The borders are slightly raised, several millimeters in width and purplish red. The inner halves of the borders of many lesions are covered with whitish fine adherent scaling and crusting. On diascopic pressure some patches do not reveal any change while others show only partial fading.

Routine laboratory tests are normal except for a relative lymphocytosis, the hemogram showing 23 polymorphonuclear eosinophils.

Patch tests gave only a 1 plus reaction to a recently prepared ointment of 30 per cent potassium iodide in petrolatum. Ingestion of 10 Gm. of potassium iodide in two doses produced a new crop of lesions, particularly in the nares, the following day.



The histologic section, examined by Dr Charles F Sims, was interpreted as "consistent with a possible dermatitis herpetiformis" The description follows "The epidermis is somewhat irregular, and at several points of the dermalepidermal junctions one may note subepidermic vesiculation Basal cell liquefaction as well as exocytosis and exocrosis is present The cells consist of small round polymorphonuclear neutrophils and an occasional eosinophil Interstitial and parenchymatous edema of the upper collagen may be noted"

## DISCUSSION

DR GEORGE C ANDREWS This case fits into the group both histologically and clinically It is hard to say whether to call it that or erythema annulare centrifugum, which it resembles a little more closely clinically, or whether to call it dermatitis herpetiformis I do not see at this time any evidence of mycosis fungoides, but it is possible that something like that may develop in the future

DR MAURICE J COSTELLO I agree with the diagnosis as presented The late Henry Niles often spoke of a patient with an eruption similar to this which cleared under intramuscular injections of bismuth subsalicylate

DR GEORGE M LEWIS I do not think that drugs can be entirely ruled out, even with a noncontributory history Since the lesions are atypical for erythema multiforme, I am in favor of an attempt to get more history in regard to drugs The presenting diagnosis is the most workable for the time being, but the cause should be looked for in drugs, bacteria or some unknown cause

DR PAUL E BECHET The annular formation is certainly suggestive of erythema multiforme However, the annular lesions, particularly about the buttocks are distinctly grouped, their borders seem raised and there is a suspicious moisture on a few of them, some of which appear vesicular It struck me that the possibility of a dermatitis herpetiformis should also be considered

DR FRANK C COMBES I agree with the diagnosis as presented I do not think that this is either erythema perstans of Darier or dermatitis herpetiformis

DR FRED WISE The tests with 30 per cent of potassium bromide and iodide ointments were only faintly positive, but the eruption flared up after ingestion of potassium iodide Many vesicular and bullous diseases are prone to become intensified from ingestion of iodides and bromides In dermatitis herpetiformis the cutaneous test with ointment is of some significance, but it should not be overvalued

## Book Reviews

**Electrotherapy and Light Therapy with the Essentials of Hydrotherapy and Mechanotherapy** By Richard Kovacs, M.D. Professor of Physical Therapy, New York Polyclinic Medical School and Hospital, New York. Fifth edition. Cloth. Price \$8.50. Pp 694, with 353 illustrations. Philadelphia: Lea & Febiger, 1945.

The fifth volume of Kovacs's excellent book dealing with many aspects of physical medicine is most welcome. As the title implies, special emphasis is placed on electrotherapy and light therapy though consideration is also given to hydrotherapy and mechanotherapy. In this edition, a new chapter on hypothermy has been added. The important subjects of roentgen and radium therapy have not been included. All chapters have been revised and brought up to date and 87 new illustrations have been added and 49 obsolete ones deleted.

The book is divided into five parts with thirty-seven chapters. Part I discusses fundamental electrophysics and the general conversion and distribution of electricity. Any physicians interested in physical medicine including the dermatologist, should read this part of the book with great care. The subject is explained in an understandable manner and is well illustrated with diagrams and drawings. Indeed, the entire volume has a wealth of illustrations, including photographs of apparatus. The author has frequently clarified the subject of electricity by comparing it with the flow of water through pipes. One subject about which the average dermatologist knows little namely the effect of cold in producing frost bite and chilblains, is well discussed under the subject of hypothermy.

Part V, dealing with applied physical therapy has chapters relating to the use of physical mediums in various specialties. The chapter on dermatologic conditions has brief descriptions of twenty-five diseases and an extended discussion of the treatment of hypertrichosis, both by electrolysis and by the high frequency current. Most of the statements in this chapter are well known to the average dermatologist and few criticisms can be made of the conservative statements of the author. This reviewer however, doubts the efficacy of radiation from a cold quartz mercury vapor lamp in improving the appearance of post-scarring. In the average case of seborrheic keratosis there is rarely need of "thorough desiccation," as in most cases a cure without scarring can be achieved by simply using a sharp curet. The author's statement that "all forms of generalized dermatitis as a rule serve as a contraindication to ultraviolet irradiation" is certainly not true in the reviewer's opinion. Excellent results may be obtained by this method in many cases of generalized eczema and psoriasis.

The great amount of information in the text, in addition to a wealth of excellent illustrations, bibliographies and glossary, makes this a most valuable book for students and practitioners of physical medicine.

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disappearing within half an hour. There were no signs of erythema or vesiculation at the test sites the following day.

The patient has not been returned to the trinitrotoluene area and has remained free from urticaria with the exception of a mild recurrence which occurred when she sat at the table with workers who had just come from the trinitrotoluene area without changing clothes.

#### COMMENT

The usual picture seen in trinitrotoluene dermatitis is a vesicular eruption on the exposed parts. Also, eczematoid and scarlatiniform eruptions are not uncommon. However, this is the first time that we have observed urticaria attributable to trinitrotoluene. At the onset, it was believed that the dermatosis might have been caused by the medications which she had taken for the infections of the upper respiratory tract. However, she continued to have urticaria after the medication was discontinued, and the onset and character of the eruption after the application of patch tests of trinitrotoluene certainly indicate that the trinitrotoluene was responsible for the reaction. It can only be conjectured whether the asthmatic signs and symptoms were related to trinitrotoluene.

# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

TREATMENT OF SOFT WARTS WITH PODOPHYLLIN J V MACGREGOR, Brit M J  
1 593 (April 28) 1945

Twenty-five patients with single or multiple condyloma acuminata of the penis or anus were successfully treated with 25 per cent podophyllum in liquid petrolatum. Isolated warts shriveled and became yellow within twenty-four hours and dropped off in a few days without ulceration or scarring.

Profuse growths usually require two or three applications. Multiple warts of the face were also cured.

The suspension must be thoroughly applied and must remain in contact with the warts for at least six to eight hours without being absorbed into or rubbed off by bandages or clothing.

"ECZEMA AUTOLYTICA" [Sic] S WATSON SMITH, Brit M J 1 628 (May 5)  
1945

The author describes a syndrome which is characterized by the initial appearance of a persisting dermatitis or ulceration or patch of varicose eczema, usually of the legs or ankle, which suddenly becomes sharply inflamed, following the eruption there is an acute eruption of scattered vesicles breaking out rapidly on the forearms, neck, face and trunk from above downward in that order.

This he calls "eczema autolytica" [eczema autolyticum], which he ascribes to the formation of a dermolysin which is frequently excited by mistreatment of the original patch of dermatitis. This tissue breakdown product then sensitizes the patient to his own exudate and is the trigger that fires the systemic outbreak. It seems certain that the lysin is blood borne and toxic rather than micro-organismal. Treatment must first be directed toward the primary lesion on the extremity, which is accomplished by elevation and local application of wet dressings followed by mild antiseptics and tight bandages. The generalized eruption fades spontaneously. Administration of sedatives, nonspecific protein and dilute hydrochloric acid and use of a lactovegetarian and salt-free diet are helpful.

SHAW, Chattanooga, Tenn

DERMATITIS FOLLOWING THE LOCAL APPLICATION OF SULPHANILAMIDE B FISHER,  
M J Australia 2 449 (Oct 28) 1944

In cases of dermatitis following the local application of sulfanilamide, weeping areas were painted daily with a 5 per cent solution of silver nitrate. All other affected areas were painted daily with a 1 per cent alcoholic solution of gentian violet medicinal. Eusol compresses were applied to areas where the dermatitis was papular. Erythema and pruritus were treated with zinc oxide cream and a 1 per cent solution of phenol.

THE INTENSIVE TREATMENT OF SYPHILIS AND OBSERVATIONS ON SEROLOGICAL REACTIONS NEIL W FRANCIS and JAMES S WANNAN, M J Australia 1 189  
(Feb 24) 1945

Some 40 patients with syphilis had been treated by the intravenous drip method, with no apparent complications, when 1 patient died from encephalitis hemorrhagica (arsenical). False positive reactions can be suspected when there is no history or clinical signs of syphilis and when contradictory results are obtained by complement fixation and flocculation tests. The titer of serum giving these false positive

It was of interest to determine approximately the ratio of dermatophytes to saprophytic fungi at which the dermatophyte would develop on the ordinary Sabouraud dextrose agar. When an inoculum of 344 T purpureum was combined with decreasing amounts of A niger, the following results were obtained (table 2, part B). Growth of the dermatophyte did not occur when the ratio was approximately 3 or less T purpureum to 1 A niger. When the ratio was about 29 of the dermatophyte to 1 A niger the dermatophyte showed growth on the unadjusted medium.

TABLE 2—*Predominance of A Niger or T Purpureum When Inoculated Together in Varying Amounts in Sabouraud's Dextrose Agar and the Alkaline Medium*

Four plates incubated five days at 34 C

A Decreasing Amounts of T Purpureum Plus a Constant Inoculum of A Niger on the Alkaline Medium			
Amounts of Cultures		Alkaline Medium	
A niger + T purpureum			
124,000 +	3,440	Pathogen (dermatophytes)	Excellent growth
		Nonpathogen (saprophytes)	Slight growth
124,000 +	344	Pathogen (dermatophytes)	No growth
		Nonpathogen (saprophytes)	Very good growth
B Constant Inoculum of T Purpureum Plus Decreasing Amounts of A Niger on Sabouraud's Dextrose Agar			
		Sabouraud's Dextrose Agar	
1,240,000 +	344	Pathogen (dermatophytes)	No growth
		Nonpathogen (saprophytes)	Excellent growth
124,000 +	344	Pathogen (dermatophytes)	No growth
		Nonpathogen (saprophytes)	Excellent growth
12,400 +	344	Pathogen (dermatophytes)	No growth
		Nonpathogen (saprophytes)	Excellent growth
1,240 +	344	Pathogen (dermatophytes)	No growth
		Nonpathogen (saprophytes)	Excellent growth
124 +	344	Pathogen (dermatophytes)	No growth
		Nonpathogen (saprophytes)	Excellent growth
12 +	344	Pathogen (dermatophytes)	Very good growth
		Nonpathogen (saprophytes)	Good growth

*Isolation from Inoculated Worn Leather*—As the alkaline medium was to be used for the recovery of pathogenic fungi from unsterile insoles of worn shoes, dermatophytes were combined with leather, and their isolation was attempted with the use of Sabouraud's maltose agar and the alkaline medium. Leather disks of 1 inch (2.5 cm) diameter were cut from worn insoles and divided into two equal halves. One half of the disk was cut into small pieces and these were suspended in water, counts were made of the growth from both Sabouraud's maltose agar and the alkaline medium. A dilute suspension of T gypsum 2 was then made and plated on both mediums. The remaining half



of the disk from the cut insole was placed in a 10 cc dilution bottle containing the dilute suspension of T gypsum 2 and was shaken with glass beads, the resulting suspension was plated. The results are shown in table 3. The counts<sup>22</sup> of the suspension of T gypsum 2 showed 14 colonies on a 1 to 100 plate of the alkaline

TABLE 3—*A Comparison Between Sabouraud's Maltose Agar and the Alkaline Medium as to Their Selective Action on a Mixture of T Gypsum 2 and Worn Insole Leather Used as Source of Varied Saprophytic Flora*

Four plates incubated at 34 C

Material Examined	Plate Dilution	Sabouraud's Maltose Agar		
		pH 5.5		pH 10.5
		Days Incubation		Days Incubation
		5	5	11
		Mold Colonies per Plate	Mold Colonies per Plate	Mold Colonies per Plate
Suspension of leather alone	1 100	25 green, 1/2 of plate covered with Aspergillus	Many small colonies of green Penicillium	Many small colonies of green Penicillium
	1 1,000	Agar completely covered with green mold	41 green	41 green
	1 10,000	6 green, 1 Aspergillus	Few green, 1 white	All green
Suspension of T gypsum 2 culture	1 100	Contaminated	14	14
	1 1,000	0	0	0
	1 10,000	0	0	0
Suspension of T gypsum 2 plus leather	1 100	Agar covered with green and black molds	32 white (pathogens)	White mold overgrowing green
	1 1,000	4 green, 1/4 plate covered with black mold	10 white (pathogens), 18 green	17 white, white mold overgrowing green
	1 10,000	0	2 white (pathogens), 7 green	1 white, 30 green, white mold overgrowing green

medium after both five and eleven days' incubation at 34 C. The unadjusted plates were contaminated, and no count of the suspension was obtained on this medium. The platings of the leather suspension showed Penicillium and Aspergillus on unadjusted agar and only Penicillium on the alkaline medium. Platings of the suspension of leather and T gypsum 2 showed only Aspergillus and Penicillium on Sabour-

<sup>22</sup> Counts were made by the dilution plate method although the inaccuracies of this method for fungi are recognized.

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